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(54) Title: METHOD FOR DISTINGUISHING IMMUNOLOGICALLY DEFINED ALL SUBTYPES

(57) Abstract: Disclosed is a method for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample by determining the expression level of markers, as well as a diagnostic kit and an apparatus containing the markers.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE:

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>KOHLMANN A ET AL: "MOLECULAR CHARACTERIZATION OF ACUTE LEUKEMIAS BY USE OF MICROARRAY TECHNOLOGY" GENES, CHROMOSOMES & CANCER, XX, XX, vol. 37, no. 4, August 2003 (2003-08), pages 396-405, XP008025253 the whole document in particular table 3</p> <p>----- -/-</p>	1-27

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TSUTSUMI SHUICHI ET AL: "Two distinct gene expression signatures in pediatric acute lymphoblastic leukemia with MLL rearrangements." CANCER RESEARCH, vol. 63, no. 16, 15 August 2003 (2003-08-15), pages 4882-4887, XP002272402 ISSN: 0008-5472 (ISSN print) the whole document	1-27
Y	YEOH E-J ET AL: "Classification, subtype discovery, and prediction of outcome in pediatric acute lymphoblastic leukemia by gene expression profiling" CANCER CELL, XX, US, vol. 1, no. 2, March 2002 (2002-03), pages 133-143, XP002253604 ISSN: 1535-6108 the whole document	1-27
Y	WO 03/039443 A (DEUTSCHES KREBSFORSCH ;HAERLACH FORSTEN (DE); EILS ROLAND (DE); K) 15 May 2003 (2003-05-15) the whole document in particular pages 71 and 72	1-27
Y	WO 03/083140 A (WONG LIMSOON ;YEOH ENG-JUH (SG); DOWNING JAMES R (US); WILKINS DAW) 9 October 2003 (2003-10-09) the whole document	1-27
Y	CHEN JIANN-SHIUH ET AL: "Identification of novel markers for monitoring minimal residual disease in acute lymphoblastic leukemia" BLOOD, vol. 97, no. 7, 1 April 2001 (2001-04-01), pages 2115-2120, XP002272403 ISSN: 0006-4971 the whole document	1-27
Y	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "Functionally Annotated Gene Expression Profiles of t(9;22) Positive CML and ALL." XP002272404 Database accession no. PREV200300335812 abstract	1-27

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	<p>& BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 1212, 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971</p>	
Y	<p>EP 1 043 676 A (WHITEHEAD BIOMEDICAL INST) 11 October 2000 (2000-10-11) the whole document</p>	1-27
Y	<p>GOLUB T R ET AL: "Molecular classification of cancer: Class discovery and class prediction by gene expression monitoring" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 286, no. 5439, 15 October 1999 (1999-10-15), pages 531-537, XP002207658 ISSN: 0036-8075 cited in the application the whole document</p>	1-27
Y	<p>DUGAS M ET AL: "A comprehensive leukemia database: integration of cytogenetics, molecular genetics and microarray data with clinical information, cytomorphology and immunophenotyping" LEUKEMIA, MACMILLAN PRESS LTD, US, vol. 15, no. 12, December 2001 (2001-12), pages 1805-1810, XP002263731 ISSN: 0887-6924 the whole document</p>	1-27
Y	<p>DUGAS MARTIN ET AL: "Impact of integrating clinical and genetic information." IN SILICO BIOLOGY, vol. 2, no. 3, 2002, pages 383-391, XP001179418 ISSN: 1386-6338 (ISSN print) the whole document</p>	1-27
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ALIZADEH A ET AL: "THE LYMPHOCHIP: A SPECIALIZED CDNA MICROARRAY FOR THE GENOMIC-SCALE ANALYSIS OF GENE EXPRESSION IN NORMAL AND MALIGNANT LYMPHOCYTES" COLD SPRING HARBOR SYMPOSIA ON QUANTITATIVE BIOLOGY, BIOLOGICAL LABORATORY, COLD SPRING HARBOR, NY, US, vol. 64, no. 1, 1999, pages 71-78, XP001099007 ISSN: 0091-7451 the whole document</p>	1-27
A	<p>DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 16 November 2002 (2002-11-16), KOHLMANN ALEXANDER ET AL: "A Simplified and Partially Automated Target Preparation Method for Gene Expression Profiling." XP002269495 Database accession no. PREV200300367771 abstract & BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 4287, 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971</p>	1-27
A	<p>DEUTSCH J M: "Evolutionary algorithms for finding optimal gene sets in microarray prediction." BIOINFORMATICS (OXFORD), vol. 19, no. 1, January 2003 (2003-01), pages 45-52, XP002272405 ISSN: 1367-4803 the whole document</p>	1-27

INTERNATIONAL SEARCH REPORT

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Article 52 (2)(d) EPC - Presentation of information

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing immunologically defined
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-27 (partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Article 52 (2)(d) EPC - Presentation of information

The claims were only searched with regards to the underlying method of generating a reference data base for distinguishing immunologically defined ALL subtypes.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-27 (partially)

A method for distinguishing mature B-ALL from all other subtypes of immunologically defined ALL subtypes, the method comprising determining the expression level of the marker CD99. Use of said marker for the manufacture of a diagnostic. A diagnostic kit containing said marker and an apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression level of CD99.

2. claims: 1-27 (all partially)

Inventions 2-1050

Methods for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL and/or T-ALL and methods for distinguishing specific subtypes against all other subtypes and against each other, the method comprising determining individually the expression level of the markers listed in tables 1.1, positions 2-50, tables 1.2-1.6 and in table 2. Use of said markers for the manufacture of diagnostics. Diagnostic kits containing said markers and apparatus comprising a reference data bank, wherein the reference data bank is obtainable by determining the expression levels of said markers.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03039443	A	15-05-2003	EP 1308522 A1	07-05-2003
			WO 03039443 A2	15-05-2003
			EP 1470247 A2	27-10-2004
WO 03083140	A	09-10-2003	AU 2003231969 A1	13-10-2003
			WO 03083140 A2	09-10-2003
			US 2004018513 A1	29-01-2004
EP 1043676	A	11-10-2000	CA 2304876 A1	09-10-2000
			EP 1043676 A2	11-10-2000
			JP 2001017171 A	23-01-2001
			US 2003017481 A1	23-01-2003
			US 6647341 B1	11-11-2003
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(71) Applicant (for DE only): **ROCHE DIAGNOSTICS
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GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
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PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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(57) Abstract: Disclosed is a method for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample by determining the expression level of markers, as well as a diagnostic kit and an apparatus containing the markers.

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Method for distinguishing immunologically defined ALL subtypes

5 The present invention is directed to a method for distinguishing immunologically defined ALL subtypes by determining the expression level of selected marker genes.

10 Leukemias are classified into four different groups or types: acute myeloid (AML), acute lymphatic (ALL), chronic myeloid (CML) and chronic lymphatic leukemia (CLL). Within these groups, several subcategories can be identified further using a panel of standard techniques as described below. These different subcategories in leukemias are associated with varying clinical outcome and therefore are the basis for different treatment strategies. The importance of highly specific classification
15 may be illustrated in detail further for the AML as a very heterogeneous group of diseases. Effort is aimed at identifying biological entities and to distinguish and classify subgroups of AML which are associated with a favorable, intermediate or unfavorable prognosis, respectively. In 1976, the FAB classification was proposed by the French-American-British co-operative group which was based on
20 cytomorphology and cytochemistry in order to separate AML subgroups according to the morphological appearance of blasts in the blood and bone marrow. In addition, it was recognized that genetic abnormalities occurring in the leukemic blast had a major impact on the morphological picture and even more on the prognosis. So far, the karyotype of the leukemic blasts is the most important
25 independent prognostic factor regarding response to therapy as well as survival.

Usually, a combination of methods is necessary to obtain the most important information in leukemia diagnostics: Analysis of the morphology and cytochemistry of bone marrow blasts and peripheral blood cells is necessary to
30 establish the diagnosis. In some cases the addition of immunophenotyping is mandatory to separate very undifferentiated AML from acute lymphoblastic leukemia and CLL. Leukemia subtypes investigated can be diagnosed by cytomorphology alone, only if an expert reviews the smears. However, a genetic analysis based on chromosome analysis, fluorescence in situ hybridization or RT-PCR and immunophenotyping is required in order to assign all cases in to the right
35 category. The aim of these techniques besides diagnosis is mainly to determine the prognosis of the leukemia. A major disadvantage of these methods, however, is that

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5 viable cells are necessary as the cells for genetic analysis have to divide in vitro in order to obtain metaphases for the analysis. Another problem is the long time of 72 hours from receipt of the material in the laboratory to obtain the result. Furthermore, great experience in preparation of chromosomes and even more in analyzing the karyotypes is required to obtain the correct result in at least 90% of cases. Using these techniques in combination, hematological malignancies in a first approach are separated into chronic myeloid leukemia (CML), chronic lymphatic (CLL), acute lymphoblastic (ALL), and acute myeloid leukemia (AML). Within the latter three disease entities several prognostically relevant subtypes have been established. As a second approach this further sub-classification is based mainly on genetic abnormalities of the leukemic blasts and clearly is associated with different prognoses.

15 The sub-classification of leukemias becomes increasingly important to guide therapy. The development of new, specific drugs and treatment approaches requires the identification of specific subtypes that may benefit from a distinct therapeutic protocol and, thus, can improve outcome of distinct subsets of leukemia. For example, the new therapeutic drug (STI571, Imatinib) inhibits the CML specific chimeric tyrosine kinase BCR-ABL generated from the genetic defect observed in CML, the BCR-ABL-rearrangement due to the translocation between chromosomes 3 and 22 (t(9;22) (q34; q11)). In patients treated with this new drug, the therapy response is dramatically higher as compared to all other drugs that had been used so far. Another example is the subtype of acute myeloid leukemia AML M3 and its variant M3v both with karyotype t(15;17)(q22; q11-12). The introduction of a new drug (all-trans retinoic acid - ATRA) has improved the outcome in this subgroup of patient from about 50% to 85 % long-term survivors. As it is mandatory for these patients suffering from these specific leukemia subtypes to be identified as fast as possible so that the best therapy can be applied, diagnostics today must accomplish sub-classification with maximal precision. Not only for these subtypes but also for several other leukemia subtypes different treatment approaches could improve outcome. Therefore, rapid and precise identification of distinct leukemia subtypes is the future goal for diagnostics.

35 Thus, the technical problem underlying the present invention was to provide means for leukemia diagnostics which overcome at least some of the disadvantages of the

prior art diagnostic methods, in particular encompassing the time-consuming and unreliable combination of different methods and which provides a rapid assay to unambiguously distinguish one subtype from another, e.g. by genetic analysis.

5 According to Golub et al. (Science, 1999, 286, 531-7), gene expression profiles can be used for class prediction and discriminating AML from ALL samples. However, for the analysis of acute leukemias the selection of the two different subgroups was performed using exclusively morphologic-phenotypical criteria. This was only
10 descriptive and does not provide deeper insights into the pathogenesis or the underlying biology of the leukemia. The approach reproduces only very basic knowledge of cytomorphology and intends to differentiate classes. The data is not sufficient to predict prognostically relevant cytogenetic aberrations.

15 Furthermore, the international application WO-A 03/039443 discloses marker genes the expression levels of which are characteristic for certain leukemia, e.g. AML subtypes and additionally discloses methods for differentiating between the subtype of AML cells by determining the expression profile of the disclosed marker genes. However, WO-A 03/039443 does not provide guidance which set of distinct genes discriminate between two subtypes and, as such, can be routinely
20 taken in order to distinguish one ALL subtype from another.

The problem is solved by the present invention, which provides a method for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample, the method
25 comprising determining the expression level of markers selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1 and or 2,

wherein

30 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.1

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is indicative for the presence of ball when ball is distinguished from all other subtypes,

and/or wherein

5 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.2

is indicative for the presence of cpre when cpre is distinguished from all other subtypes,

10 and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 6, 8, 9, 10, 12, 13, 14, 16, 17, 18, 22, 23, 24, 25, 30, 31, 34, 38, 40, 42, 43, 44, 46, 48, and/or 49, of Table 1.3 and/or

15 a higher expression of at least one polynucleotide defined by any of the numbers 4, 5, 7, 11, 15, 19, 20, 21, 26, 27, 28, 29, 32, 33, 35, 36, 37, 39, 41, 45, 47, and/or 50 of Table 1.3

is indicative for the presence of cpreh when cpreh is distinguished from all other subtypes,

and/or wherein

20 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, and/or 48, of Table 1.4, and/or

25 a higher expression of at least one polynucleotide defined by any of the numbers 16, 22, 39, 49, and/or 50 of Table 1.4

is indicative for the presence of kort when kort is distinguished from all other subtypes,

and/or wherein

30 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.5

- 5 -

is indicative for the presence of pret when pret is distinguished from all other subtypes,

and/or wherein

5 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 6, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 25, 26, 27, 28, 29, 32, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 5, 7, 10, 20, 22, 23, 24, 30, 31, 33, 34, and/or 39 of Table 1.6,

10 is indicative for the presence of prob when prob is distinguished from from all other subtypes,

and/or wherein

15 a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 4, 8, 10, 12, 15, 17, 20, 23, 24, 25, 27, 28, 29, 30, 31, 34, 36, 37, 40, 42, 44, 45, 46, 49, and/or 50 of Table 2.1, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 5, 6, 7, 9, 11, 13, 14, 16, 18, 19, 21, 22, 26, 32, 33, 35, 38, 39, 41, 43, 47, 48,

20 is indicative for the presence of ball when ball is distinguished from cpre,

and/or wherein

25 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table of Table 2.2, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 26, and/or 37, of Table 2.2

is indicative for the presence of ball when ball is distinguished from cpreph,

30 and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21,

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22, 23, 24, 25, 26, 28, 30, 31, 33, 34, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, and/or 49, of Table 2.3, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 6, 7, 27, 29, 32, 35, 44, and/or 50 of Table 2.3

5 is indicative for the presence of ball when ball is distinguished from kort,

and/or wherein

10 a lower expression of at least one polynucleotide defined by any of the numbers 3, 5, 6, 7, 13, 17, 18, 19, 21, 22, 26, 27, 30, 32, 34, 36, 38, 40, 47, and/or 48, of Table 2.4, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 8, 9, 10, 11, 12, 14, 15, 16, 20, 23, 24, 25, 28, 29, 31, 33, 35, 37, 39, 41, 42, 43, 44, 45, 46, 49, and/or 50 of Table 2.4

15 is indicative for the presence of ball when ball is distinguished from pret,

and/or wherein

20 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table of Table 2.5, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 29, 30 and/or 39, of Table 2.5,

is indicative for the presence of ball when ball is distinguished from prob,

25 and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 7, 9, 10, 11, 13, 17, 18, 21, 24, 25, 27, 29, 30, 31, 36, 37, 38, 40, 42, 43, 45, 46, 49, and/or 50 of Table 2.6, and/or

30 a higher expression of at least one polynucleotide defined by any of the numbers 6, 8, 12, 14, 15, 16, 19, 20, 22, 23, 26, 28, 32, 33, 34, 35, 39, 41, 44, 47, and/or 48 of Table 2.6,

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is indicative for the presence of cpre when cpre is distinguished from cpreph,

and/or wherein

5 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 6, 8, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 28, 29, 30, 31, 32, 35, 36, 38, 40, 41, 43, 44, 45, 46, 48, 49, and/or 50 of Table 2.7, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 3, 7, 9, 11, 22, 26, 33, 34, 37, 39, 42, 47, of Table 2.7,

10 is indicative for cpre when cpre is distinguished from kort,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 20, 28, 31, 37, 38, and/or 50 of Table 2.8, and/or

15 a higher expression of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25, 26, 27, 29, 30, 32, 33, 34, 35, 36, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, and/or 49 of Table 2.8

is indicative for cpre when cpre is distinguished from pret,

and/or wherein

20 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, and/or 50 of Table 2.9,

a higher expression of at least one polynucleotide defined by any of the numbers 26, 33, 41, and/or 49 of Table 2.9

25 is indicative for cpre when cpre is distinguished from prob,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 3, 6, 12, 17, 23, 28, 34, 35, and/or 41, of Table 2.10, and/or

30 a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 7, 8, 9, 10, 11, 13, 14, 15, 16, 18, 19, 20, 21, 22, 24,

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25, 26, 27, 29, 30, 31, 32, 33, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.10

is indicative for cpreph when cpreph is distinguished from kort,

and/or wherein

5 a lower expression of at least one polynucleotide defined by any of the numbers 42, and/or 43, of Table 2.11, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 10 39, 40, 41, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.11,

is indicative for cpreph when cpreph is distinguished from pret,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 5, 8, 9, 11, 12, 13, 15, 18, 21, 24, 27, 28, 29, 32, 34, 36, 15 38, 41, 42, 43, 46, 47, 48, of Table 2.12, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 4, 6, 7, 10, 14, 16, 17, 19, 20, 22, 23, 25, 26, 30, 31, 33, 35, 37, 39, 40, 44, 45, 49, and/or 50 of Table 2.12

is indicative for cpreph when cpreph is distinguished from prob

20 and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 19, and/or 40, of Table 2.13

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 20, 25 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.13,

is indicative for kort when kort is distinguished from pret,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 4, 7, 9, 10, 11, 13, 14, 15, 16, 17, 20, 21, 22, 28, 29, 31, 32, 33, 35, 36, 37, 40, 41, 42, 43, 45, 47, 48, and/or 50 of Table 2.14, 30 and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 3, 5, 6, 8, 12, 18, 19, 23, 24, 25, 26, 27, 30, 34, 38, 39, 44, 46, and/or 49, of Table 2.14

is indicative for kort when kort is distinguished from prob,

5 and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.15,

10 is indicative for pret when pret is distinguished from prob.

As used herein, the following abbreviations represent the classified immunologically defined ALL subtypes:

ball=Mature B-ALL

15 cpre=c-ALL/Pre-B-ALL without t(9;22)

cpreph= c-ALL/Pre-B-ALL with t(9;22)

kort=Cortical T-ALL

pret=Pre-T-ALL

prob=Pro-B-ALL

20

According to the present invention, a "sample" means any biological material containing genetic information in the form of nucleic acids or proteins obtainable or obtained from an individual. The sample includes e.g. tissue samples, cell samples, bone marrow and/or body fluids such as blood, saliva, semen. Preferably, 25 the sample is blood or bone marrow, more preferably the sample is bone marrow. The person skilled in the art is aware of methods, how to isolate nucleic acids and proteins from a sample. A general method for isolating and preparing nucleic acids from a sample is outlined in Example 3.

30 According to the present invention, the term "lower expression" is generally assigned to all by numbers and Affymetrix Id. definable polynucleotides the t-

values and fold change (fc) values of which are negative, as indicated in the Tables. Accordingly, the term "higher expression" is generally assigned to all by numbers and Affymetrix Id. definable polynucleotides the t-values and fold change (fc) values of which are positive.

5

According to the present invention, the term "expression" refers to the process by which mRNA or a polypeptide is produced based on the nucleic acid sequence of a gene, i.e. „expression“ also includes the formation of mRNA upon transcription. In accordance with the present invention, the term „determining the expression level“
10 preferably refers to the determination of the level of expression, namely of the markers.

Generally, "marker" refers to any genetically controlled difference which can be used in the genetic analysis of a test versus a control sample, for the purpose of
15 assigning the sample to a defined genotype or phenotype. As used herein, "markers" refer to genes which are differentially expressed in, e.g., different AML subtypes. The markers can be defined by their gene symbol name, their encoded protein name, their transcript identification number (cluster identification number), the data base accession number, public accession number or GenBank identifier or,
20 as done in the present invention, Affymetrix identification number, chromosomal location, UniGene accession number and cluster type, LocusLink accession number (see Examples and Tables).

The Affymetrix identification number (affy id) is accessible for anyone and the
25 person skilled in the art by entering the "gene expression omnibus" internet page of the National Center for Biotechnology Information (NCBI) (<http://www.ncbi.nlm.nih.gov/geo/>). In particular, the affy id's of the polynucleotides used for the method of the present invention are derived from the so-called U133 chip. The sequence data of each identification number can be
30 viewed at <http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GPL96>

Generally, the expression level of a marker is determined by the determining the expression of its corresponding "polynucleotide" as described hereinafter.

According to the present invention, the term „polynucleotide“ refers, generally, to a DNA, in particular cDNA, or RNA, in particular a cRNA, or a portion thereof or a polypeptide or a portion thereof. In the case of RNA (or cDNA), the polynucleotide is formed upon transcription of a nucleotide sequence which is capable of expression. The polynucleotide fragments refer to fragments preferably of between at least 8, such as 10, 12, 15 or 18 nucleotides and at least 50, such as 60, 80, 100, 200 or 300 nucleotides in length, or a complementary sequence thereto, representing a consecutive stretch of nucleotides of a gene, cDNA or mRNA. In other terms, polynucleotides include also any fragment (or complementary sequence thereto) of a sequence derived from any of the markers defined above as long as these fragments unambiguously identify the marker.

The determination of the expression level may be effected at the transcriptional or translational level, i.e. at the level of mRNA or at the protein level. Protein fragments such as peptides or polypeptides advantageously comprise between at least 6 and at least 25, such as 30, 40, 80, 100 or 200 consecutive amino acids representative of the corresponding full length protein. Six amino acids are generally recognized as the lowest peptidic stretch giving rise to a linear epitope recognized by an antibody, fragment or derivative thereof. Alternatively, the proteins or fragments thereof may be analysed using nucleic acid molecules specifically binding to three-dimensional structures (aptamers).

Depending on the nature of the polynucleotide or polypeptide, the determination of the expression levels may be effected by a variety of methods. For determining and detecting the expression level, it is preferred in the present invention that the polynucleotide, in particular the cRNA, is labelled.

The labelling of the polynucleotide or a polypeptide can occur by a variety of methods known to the skilled artisan. The label can be fluorescent, chemiluminescent, bioluminescent, radioactive (such as ^3H or ^{32}P). The labelling compound can be any labelling compound being suitable for the labelling of polynucleotides and/or polypeptides. Examples include fluorescent dyes, such as fluorescein, dichlorofluorescein, hexachlorofluorescein, BODIPY variants, ROX, tetramethylrhodamin, rhodamin X, Cyanine-2, Cyanine-3, Cyanine-5, Cyanine-7, IRD40, FluorX, Oregon Green, Alexa variants (available e.g. from Molecular Probes or Amersham Biosciences) and the like, biotin or biotinylated nucleotides,

digoxigenin, radioisotopes, antibodies, enzymes and receptors. Depending on the type of labelling, the detection is done via fluorescence measurements, conjugation to streptavidin and/or avidin, antigen-antibody- and/or antibody-antibody-interactions, radioactivity measurements, as well as catalytic and/or receptor/ligand interactions. Suitable methods include the direct labelling (incorporation) method, the amino-modified (amino-allyl) nucleotide method (available e.g. from Ambion), and the primer tagging method (DNA dendrimer labelling, as kit available e.g. from Genisphere). Particularly preferred for the present invention is the use of biotin or biotinylated nucleotides for labelling, with the latter being directly incorporated into, e.g. the cRNA polynucleotide by in vitro transcription.

If the polynucleotide is mRNA, cDNA may be prepared into which a detectable label, as exemplified above, is incorporated. Said detectably labelled cDNA, in single-stranded form, may then be hybridised, preferably under stringent or highly stringent conditions to a panel of single-stranded oligonucleotides representing different genes and affixed to a solid support such as a chip. Upon applying appropriate washing steps, those cDNAs will be detected or quantitatively detected that have a counterpart in the oligonucleotide panel. Various advantageous embodiments of this general method are feasible. For example, the mRNA or the cDNA may be amplified e.g. by polymerase chain reaction, wherein it is preferable, for quantitative assessments, that the number of amplified copies corresponds relative to further amplified mRNAs or cDNAs to the number of mRNAs originally present in the cell. In a preferred embodiment of the present invention, the cDNAs are transcribed into cRNAs prior to the hybridisation step wherein only in the transcription step a label is incorporated into the nucleic acid and wherein the cRNA is employed for hybridisation. Alternatively, the label may be attached subsequent to the transcription step.

Similarly, proteins from a cell or tissue under investigation may be contacted with a panel of aptamers or of antibodies or fragments or derivatives thereof. The antibodies etc. may be affixed to a solid support such as a chip. Binding of proteins indicative of an AML subtype may be verified by binding to a detectably labelled secondary antibody or aptamer. For the labelling of antibodies, it is referred to Harlow and Lane, "Antibodies, a laboratory manual", CSH Press, 1988, Cold Spring Harbor. Specifically, a minimum set of proteins necessary for diagnosis of

all AML subtypes may be selected for creation of a protein array system to make diagnosis on a protein lysate of a diagnostic bone marrow sample directly. Protein Array Systems for the detection of specific protein expression profiles already are available (for example: Bio-Plex, BIORAD, München, Germany). For this application preferably antibodies against the proteins have to be produced and immobilized on a platform e.g. glasslides or microtiterplates. The immobilized antibodies can be labelled with a reactant specific for the certain target proteins as discussed above. The reactants can include enzyme substrates, DNA, receptors, antigens or antibodies to create for example a capture sandwich immunoassay.

10

For reliably distinguishing ALL subtypes it is useful that the expression of more than one of the above defined markers is determined. As a criterion for the choice of markers, the statistical significance of markers as expressed in q or p values based on the concept of the false discovery rate is determined. In doing so, a measure of statistical significance called the q value is associated with each tested feature. The q value is similar to the p value, except it is a measure of significance in terms of the false discovery rate rather than the false positive rate (Storey JD and Tibshirani R. Proc.Natl.Acad.Sci., 2003, Vol. 100:9440-5).

15

In a preferred embodiment of the present invention, markers as defined in Tables 1.1-2.15 having a q -value of less than $3E-06$, more preferred less than $1.5E-09$, most preferred less than $1.5E-11$, are measured.

20

Of the above defined markers, the expression level of at least two, preferably of at least ten, more preferably of at least 25, most preferably of 50 of at least one of the Tables of the markers is determined.

25

In another preferred embodiment, the expression level of at least 2, of at least 5, of at least 10 out of the markers having the numbers 1 – 10, 1-20, 1-40, 1-50 of at least one of the Tables 1.1-2.15 are measured.

30

The level of the expression of the „marker“, i.e. the expression of the polynucleotide is indicative of the ALL subtype of a cell or an organism. The level of expression of a marker or group of markers is measured and is compared with the level of expression of the same marker or the same group of markers from other cells or samples. The comparison may be effected in an actual experiment or in

35

silico. When the expression level also referred to as expression pattern or expression signature (expression profile) is measurably different, there is according to the invention a meaningful difference in the level of expression. Preferably the difference at least is 5 %, 10% or 20%, more preferred at least 50% or may even be as high as 75% or 100%. More preferred the difference in the level of expression is at least 200%, i.e. two fold, at least 500%, i.e. five fold, or at least 1000%, i.e. 10 fold.

Accordingly, the expression level of markers expressed lower in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold lower, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold lower in the first subtype. On the other hand, the expression level of markers expressed higher in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold higher, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold higher in the first subtype.

In another embodiment of the present invention, the sample is derived from an individual having leukaemia, preferably ALL.

For the method of the present invention it is preferred if the polynucleotide the expression level of which is determined is in form of a transcribed polynucleotide. A particularly preferred transcribed polynucleotide is an mRNA, a cDNA and/or a cRNA, with the latter being preferred. Transcribed polynucleotides are isolated from a sample, reverse transcribed and/or amplified, and labelled, by employing methods well-known to the person skilled in the art (see Example 3). In a preferred embodiment of the methods according to the invention, the step of determining the expression profile further comprises amplifying the transcribed polynucleotide.

In order to determine the expression level of the transcribed polynucleotide by the method of the present invention, it is preferred that the method comprises hybridizing the transcribed polynucleotide to a complementary polynucleotide, or a portion thereof, under stringent hybridization conditions, as described hereinafter.

The term "hybridizing" means hybridization under conventional hybridization conditions, preferably under stringent conditions as described, for example, in Sambrook, J., et al., in "Molecular Cloning: A Laboratory Manual" (1989), Eds. J. Sambrook, E. F. Fritsch and T. Maniatis, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, NY and the further definitions provided above. Such conditions are, for example, hybridization in 6x SSC, pH 7.0 / 0.1% SDS at about 45°C for 18-23 hours, followed by a washing step with 2x SSC/0.1% SDS at 50°C. In order to select the stringency, the salt concentration in the washing step can for example be chosen between 2x SSC/0.1% SDS at room temperature for low stringency and 0.2x SSC/0.1% SDS at 50°C for high stringency. In addition, the temperature of the washing step can be varied between room temperature, ca. 22°C, for low stringency, and 65°C to 70°C for high stringency. Also contemplated are polynucleotides that hybridize at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation, preferably of formamide concentration (lower percentages of formamide result in lowered stringency), salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH₂PO₄; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 mg/ml salmon sperm blocking DNA, followed by washes at 50°C with 1 X SSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5x SSC). Variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

"Complementary" and "complementarity", respectively, can be described by the percentage, i.e. proportion, of nucleotides which can form base pairs between two polynucleotide strands or within a specific region or domain of the two strands. Generally, complementary nucleotides are, according to the base pairing rules, adenine and thymine (or adenine and uracil), and cytosine and guanine. Complementarity may be partial, in which only some of the nucleic acids' bases are matched according to the base pairing rules. Or, there may be a complete or total complementarity between the nucleic acids. The degree of complementarity

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between nucleic acid strands has effects on the efficiency and strength of hybridization between nucleic acid strands.

Two nucleic acid strands are considered to be 100% complementary to each other over a defined length if in a defined region all adenines of a first strand can pair with a thymine (or an uracil) of a second strand, all guanines of a first strand can pair with a cytosine of a second strand, all thymine (or uracils) of a first strand can pair with an adenine of a second strand, and all cytosines of a first strand can pair with a guanine of a second strand, and vice versa. According to the present invention, the degree of complementarity is determined over a stretch of 20, preferably 25, nucleotides, i.e. a 60% complementarity means that within a region of 20 nucleotides of two nucleic acid strands 12 nucleotides of the first strand can base pair with 12 nucleotides of the second strand according to the above ruling, either as a stretch of 12 contiguous nucleotides or interspersed by non-pairing nucleotides, when the two strands are attached to each other over said region of 20 nucleotides. The degree of complementarity can range from at least about 50% to full, i.e. 100% complementarity. Two single nucleic acid strands are said to be "substantially complementary" when they are at least about 80% complementary, preferably about 90% or higher. For carrying out the method of the present invention substantial complementarity is preferred.

Preferred methods for detection and quantification of the amount of polynucleotides, i.e. for the methods according to the invention allowing the determination of the level of expression of a marker, are those described by Sambrook et al. (1989) or real time methods known in the art as the TaqMan® method disclosed in WO92/02638 and the corresponding U.S. 5,210,015, U.S. 5,804,375, U.S. 5,487,972. This method exploits the exonuclease activity of a polymerase to generate a signal. In detail, the (at least one) target nucleic acid component is detected by a process comprising contacting the sample with an oligonucleotide containing a sequence complementary to a region of the target nucleic acid component and a labeled oligonucleotide containing a sequence complementary to a second region of the same target nucleic acid component sequence strand, but not including the nucleic acid sequence defined by the first oligonucleotide, to create a mixture of duplexes during hybridization conditions, wherein the duplexes comprise the target nucleic acid annealed to the first oligonucleotide and to the labeled oligonucleotide such that the 3'-end of the first oligonucleotide is adjacent to the 5'-end of the labeled oligonucleotide. Then this

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mixture is treated with a template-dependent nucleic acid polymerase having a 5' to 3' nuclease activity under conditions sufficient to permit the 5' to 3' nuclease activity of the polymerase to cleave the annealed, labeled oligonucleotide and release labeled fragments. The signal generated by the hydrolysis of the labeled oligonucleotide is detected and/ or measured. TaqMan® technology eliminates the need for a solid phase bound reaction complex to be formed and made detectable. Other methods include e.g. fluorescence resonance energy transfer between two adjacently hybridized probes as used in the LightCycler® format described in U.S. 6,174,670.

A preferred protocol if the marker, i.e. the polynucleotide, is in form of a transcribed nucleotide, is described in Example 3, where total RNA is isolated, cDNA and, subsequently, cRNA is synthesized and biotin is incorporated during the transcription reaction. The purified cRNA is applied to commercially available arrays which can be obtained e.g. from Affymetrix. The hybridized cRNA is detected according to the methods described in Example 3. The arrays are produced by photolithography or other methods known to experts skilled in the art e.g. from U.S. 5,445,934, U.S. 5,744,305, U.S. 5,700,637, U.S. 5,945,334 and EP 0 619 321 or EP 0 373 203, or as described hereinafter in greater detail.

In another embodiment of the present invention, the polynucleotide or at least one of the polynucleotides is in form of a polypeptide. In another preferred embodiment, the expression level of the polynucleotides or polypeptides is detected using a compound which specifically binds to the polynucleotide of the polypeptide of the present invention.

As used herein, "specifically binding" means that the compound is capable of discriminating between two or more polynucleotides or polypeptides, i.e. it binds to the desired polynucleotide or polypeptide, but essentially does not bind unspecifically to a different polynucleotide or polypeptide.

The compound can be an antibody, or a fragment thereof, an enzyme, a so-called small molecule compound, a protein-scaffold, preferably an anticalin. In a preferred embodiment, the compound specifically binding to the polynucleotide or polypeptide is an antibody, or a fragment thereof.

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As used herein, an "antibody" comprises monoclonal antibodies as first described by Köhler and Milstein in Nature 278 (1975), 495-497 as well as polyclonal antibodies, i.e. antibodies contained in a polyclonal antiserum. Monoclonal antibodies include those produced by transgenic mice. Fragments of antibodies include F(ab')₂, Fab and Fv fragments. Derivatives of antibodies include scFvs, chimeric and humanized antibodies. See, for example Harlow and Lane, loc. cit. For the detection of polypeptides using antibodies or fragments thereof, the person skilled in the art is aware of a variety of methods, all of which are included in the present invention. Examples include immunoprecipitation, Western blotting, Enzyme-linked immuno sorbent assay (ELISA), Enzyme-linked immuno sorbent assay (RIA), dissociation-enhanced lanthanide fluoro immuno assay (DELFI), scintillation proximity assay (SPA). For detection, it is desirable if the antibody is labelled by one of the labelling compounds and methods described supra.

In another preferred embodiment of the present invention, the method for distinguishing immunologically defined ALL subtypes is carried out on an array.

In general, an "array" or "microarray" refers to a linear or two- or three dimensional arrangement of preferably discrete nucleic acid or polypeptide probes which comprises an intentionally created collection of nucleic acid or polypeptide probes of any length spotted onto a substrate/solid support. The person skilled in the art knows a collection of nucleic acids or polypeptide spotted onto a substrate/solid support also under the term "array". As known to the person skilled in the art, a microarray usually refers to a miniaturised array arrangement, with the probes being attached to a density of at least about 10, 20, 50, 100 nucleic acid molecules referring to different or the same genes per cm². Furthermore, where appropriate an array can be referred to as "gene chip". The array itself can have different formats, e.g. libraries of soluble probes or libraries of probes tethered to resin beads, silica chips, or other solid supports.

The process of array fabrication is well-known to the person skilled in the art. In the following, the process for preparing a nucleic acid array is described. Commonly, the process comprises preparing a glass (or other) slide (e.g. chemical treatment of the glass to enhance binding of the nucleic acid probes to the glass surface), obtaining DNA sequences representing genes of a genome of interest, and

spotting sequences these sequences of interest onto glass slide. Sequences of interest can be obtained via creating a cDNA library from an mRNA source or by using publicly available databases, such as GeneBank, to annotate the sequence information of custom cDNA libraries or to identify cDNA clones from previously prepared libraries. Generally, it is recommendable to amplify obtained sequences by PCR in order to have sufficient amounts of DNA to print on the array. The liquid containing the amplified probes can be deposited on the array by using a set of microspotting pins. Ideally, the amount deposited should be uniform. The process can further include UV-crosslinking in order to enhance immobilization of the probes on the array.

In a preferred embodiment, the array is a high density oligonucleotide (oligo) array using a light-directed chemical synthesis process, employing the so-called photolithography technology. Unlike common cDNA arrays, oligo arrays (according to the Affymetrix technology) use a single-dye technology. Given the sequence information of the markers, the sequence can be synthesized directly onto the array, thus, bypassing the need for physical intermediates, such as PCR products, required for making cDNA arrays. For this purpose, the marker, or partial sequences thereof, can be represented by 14 to 20 features, preferably by less than 14 features, more preferably less than 10 features, even more preferably by 6 features or less, with each feature being a short sequence of nucleotides (oligonucleotide), which is a perfect match (PM) to a segment of the respective gene. The PM oligonucleotide are paired with mismatch (MM) oligonucleotides which have a single mismatch at the central base of the nucleotide and are used as "controls". The chip exposure sites are defined by masks and are deprotected by the use of light, followed by a chemical coupling step resulting in the synthesis of one nucleotide. The masking, light deprotection, and coupling process can then be repeated to synthesize the next nucleotide, until the nucleotide chain is of the specified length.

Advantageously, the method of the present invention is carried out in a robotics system including robotic plating and a robotic liquid transfer system, e.g. using microfluidics, i.e. channelled structured.

A particular preferred method according to the present invention is as follows:

1. Obtaining a sample, e.g. bone marrow or peripheral blood aliquots, from a patient having ALL

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2. Extracting RNA, preferably mRNA, from the sample
3. Reverse transcribing the RNA into cDNA
4. In vitro transcribing the cDNA into cRNA
5. Fragmenting the cRNA
- 5 6. Hybridizing the fragmented cRNA on standard microarrays
7. Determining hybridization

10 In another embodiment, the present invention is directed to the use of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2 for the manufacturing of a diagnostic for distinguishing immunologically defined ALL subtypes. The use of the present invention is particularly advantageous for distinguishing immunologically defined ALL subtypes in an individual having ALL. The use of said markers for diagnosis of immunologically defined leukemia subtypes, 15 preferably based on microarray technology, offers the following advantages: (1) more rapid and more precise diagnosis, (2) easy to use in laboratories without specialized experience, (3) abolishes the requirement for analyzing viable cells for chromosome analysis (transport problem), and (4) very experienced hematologists for cytomorphology and cytochemistry, immunophenotyping as well as 20 cytogeneticists and molecularbiologists are no longer required.

Accordingly, the present invention refers to a diagnostic kit containing at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2 for distinguishing 25 immunologically defined ALL subtypes, in combination with suitable auxiliaries. Suitable auxiliaries, as used herein, include buffers, enzymes, labelling compounds, and the like. In a preferred embodiment, the marker contained in the kit is a nucleic acid molecule which is capable of hybridizing to the mRNA corresponding to at least one marker of the present invention. Preferably, the at least one nucleic acid 30 molecule is attached to a solid support, e.g. a polystyrene microtiter dish, nitrocellulose membrane, glass surface or to non-immobilized particles in solution.

In another preferred embodiment, the diagnostic kit contains at least one reference for a Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, 35 precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL subtype. As used herein, the reference can be a sample or a data bank.

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In another embodiment, the present invention is directed to an apparatus for distinguishing immunologically defined AML subtypes subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample, containing a reference data bank obtainable by comprising

- (a) compiling a gene expression profile of a patient sample by determining the expression level at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2, and
- (b) classifying the gene expression profile by means of a machine learning algorithm.

According to the present invention, the "machine learning algorithm" is a computational-based prediction methodology, also known to the person skilled in the art as "classifier", employed for characterizing a gene expression profile. The signals corresponding to a certain expression level which are obtained by the microarray hybridization are subjected to the algorithm in order to classify the expression profile. Supervised learning involves "training" a classifier to recognize the distinctions among classes and then "testing" the accuracy of the classifier on an independent test set. For new, unknown sample the classifier shall predict into which class the sample belongs.

Preferably, the machine learning algorithm is selected from the group consisting of Weighted Voting, K-Nearest Neighbors, Decision Tree Induction, Support Vector Machines (SVM), and Feed-Forward Neural Networks. Most preferably, the machine learning algorithm is Support Vector Machine, such as polynomial kernel and Gaussian Radial Basis Function-kernel SVM models.

The classification accuracy of a given gene list for a set of microarray experiments is preferably estimated using Support Vector Machines (SVM), because there is evidence that SVM-based prediction slightly outperforms other classification techniques like k-Nearest Neighbors (k-NN). The LIBSVM software package version 2.36 was used (SVM-type: C-SVC, linear kernel (<http://www.csie.ntu.edu.tw/~cjlin/libsvm/>)). The skilled artisan is furthermore referred to Brown et al., Proc.Natl.Acad.Sci., 2000; 97: 262-267, Furey et al., Bioinformatics. 2000; 16: 906-914, and Vapnik V. Statistical Learning Theory. New York: Wiley, 1998.

In detail, the classification accuracy of a given gene list for a set of microarray experiments can be estimated using Support Vector Machines (SVM) as supervised learning technique. Generally, SVMs are trained using differentially expressed genes which were identified on a subset of the data and then this trained model is employed to assign new samples to those trained groups from a second and different data set. Differentially expressed genes were identified applying ANOVA and t-test-statistics (Welch t-test). Based on identified distinct gene expression signatures respective training sets consisting of 2/3 of cases and test sets with 1/3 of cases to assess classification accuracies are designated. Assignment of cases to training and test set is randomized and balanced by diagnosis. Based on the training set a Support Vector Machine (SVM) model is built.

According to the present invention, the apparent accuracy, i.e. the overall rate of correct predictions of the complete data set was estimated by 10fold cross validation. This means that the data set was divided into 10 approximately equally sized subsets, an SVM-model was trained for 9 subsets and predictions were generated for the remaining subset. This training and prediction process was repeated 10 times to include predictions for each subset. Subsequently the data set was split into a training set, consisting of two thirds of the samples, and a test set with the remaining one third. Apparent accuracy for the training set was estimated by 10fold cross validation (analogous to apparent accuracy for complete set). A SVM-model of the training set was built to predict diagnosis in the independent test set, thereby estimating true accuracy of the prediction model. This prediction approach was applied both for overall classification (multi-class) and binary classification (diagnosis X \Rightarrow yes or no). For the latter, sensitivity and specificity were calculated:

Sensitivity = (number of positive samples predicted)/(number of true positives)

Specificity = (number of negative samples predicted)/(number of true negatives)

In a preferred embodiment, the reference data bank is backed up on a computational data memory chip which can be inserted in as well as removed from the apparatus of the present invention, e.g. like an interchangeable module, in order to use another data memory chip containing a different reference data bank.

The apparatus of the present invention containing a desired reference data bank can be used in a way such that an unknown sample is, first, subjected to gene expression profiling, e.g. by microarray analysis in a manner as described supra or in the art, and the expression level data obtained by the analysis are, second, fed
5 into the apparatus and compared with the data of the reference data bank obtainable by the above method. For this purpose, the apparatus suitably contains a device for entering the expression level of the data, for example a control panel such as a keyboard. The results, whether and how the data of the unknown sample fit into the reference data bank can be made visible on a provided monitor or display screen
10 and, if desired, printed out on an incorporated or connected printer.

Alternatively, the apparatus of the present invention is equipped with particular appliances suitable for detecting and measuring the expression profile data and, subsequently, proceeding with the comparison with the reference data bank. In this
15 embodiment, the apparatus of the present invention can contain a gripper arm and/or a tray which takes up the microarray containing the hybridized nucleic acids.

In another embodiment, the present invention refers to a reference data bank for
20 distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample obtainable by comprising

- 25 (a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or and
- (b) classifying the gene expression profile by means of a machine learning algorithm.

30 Preferably, the reference data bank is backed up and/or contained in a computational memory data chip.

The invention is further illustrated in the following table and examples, without limiting the scope of the invention:

TABLES 1.1-2.15

Tables 1.1-2.15 show ALLL subtype analysis of subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL. The analysed markers are ordered according to their q-values, beginning with the lowest q-values.

For convenience and a better understanding, Tables 1.1 to 2.15 are accompanied with explanatory tables (Table 1.1A to 2.15A) where the numbering and the Affymetrix Id are further defined by other parameters, e.g. gene bank accession number.

EXAMPLES

Example 1: General experimental design of the invention and results

Acute lymphoblastic leukemia (ALL) is a heterogeneous group of diseases which are classified immunologically. Most of the clinically relevant subgroups are characterized by specific genetic translocations, i.e. translocations involving MLL (t(MLL) in Pro-B-ALL, t(9;22) in c-ALL and Pre-B-ALL, and t(8;14) in mature B-ALL. While in childhood ALL gene expression profiling revealed specific gene signatures in cytogenetically defined subgroup the respective data are scarce in adult ALL and, in particular, it is not known if the immunologically defined subtypes of ALL which lack specific cytogenetic aberrations display a characteristic gene expression profile. We analyzed global gene expression signatures in bone marrow samples from 95 patients with newly diagnosed ALL by use of microarray technology (Pro-B-ALL n=18, c-ALL n=18, Pre-B-ALL n=5, c-ALL/Pre-B-ALL n=12, mature B-ALL n=11, precursor B-ALL n=3, Pro-T-ALL n=2, Pre-T-ALL n=8, cortical T-ALL n=14, mature T-ALL n=2, T-ALL n=2). The diagnosis was based on cytomorphology, immunophenotyping, and cytogenetic and molecular genetic analyses. All samples were hybridized onto U133 set microarrays (Affymetrix) representing >30,000 human transcripts. Differentially expressed genes were identified applying ANOVA and t-test-statistics (Welch ttest). To assess the false discovery rate we calculated q-values according to Storey et al., PNAS 2003. Moreover, based on identified distinct gene expression

signatures we designated respective training sets consisting of 2/3 of cases and test samples with 1/3 of cases to assess classification accuracies. Assignment of cases to training and test set was randomized and balanced by diagnosis. Based on the training set we built a Support Vector Machine (SVM) model. Classification accuracy was assessed in the test set. In a first step, precursor B-ALL and precursor T-ALL were distinguished in 31 independent test samples with an accuracy of 100%. In a second step samples were separated according to the EGIL classification (Pro-B-ALL, c-ALL, Pre-B-ALL, mature B-ALL, Pre-T-ALL, cortical T-ALL). Out of the 25 test samples 20 were classified correctly (accuracy: 80%). Samples misclassified were: c-ALL as Pre-B-ALL (n=2), c-ALL as mature B-ALL, cortical T-ALL as Pre-T-ALL, and Pre-B-ALL as mature B-ALL (one each). Samples with c-ALL and Pre-B-ALL were then further subgrouped genetically according to positivity/negativity for t(9;22). Out of 29 test samples 24 were classified correctly (accuracy: 83%). Sample misclassified were: c-ALL/Pre-B-ALL without t(9;22) as Pro-B-ALL and mature B-ALL (one each), c-ALL/Pre-B-ALL with t(9;22) as c-ALL/Pre-B-ALL without t(9;22) and mature B-ALL (one each), Pre-T-ALL as cortical T-ALL. These data demonstrate that distinct immunologically defined subtypes of ALL are characterized by specific gene expression profiles. Distinction between T-lineage and B-lineage disease is accomplished with 100% accuracy while misclassification occurs in cases belonging to subtypes closely related to each other with regard to the maturation status. Gene expression profiling of ALL may help to optimize diagnostics of ALL and to allow further insights into the pathogenesis of the biologically defined subgroups.

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Example 2: General materials, methods and definitions of functional annotations

The methods section contains both information on statistical analyses used for identification of differentially expressed genes and detailed annotation data of identified microarray probesets.

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Affymetrix Probeset Annotation

All annotation data of GeneChip® arrays are extracted from the NetAffx™ Analysis Center (internet website: www.affymetrix.com). Files for U133 set arrays, including U133A and U133B microarrays are derived from the June 2003 release.

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The original publication refers to: Liu G, Loraine AE, Shigeta R, Cline M, Cheng J, Valmeekam V, Sun S, Kulp D, Siani-Rose MA. NetAffx: Affymetrix probesets and annotations. Nucleic Acids Res. 2003;31(1):82-6.

5 The sequence data are omitted due to their large size, and because they do not change, whereas the annotation data are updated periodically, for example new information on chromosomal location and functional annotation of the respective gene products. Sequence data are available for download in the NetAffx Download Center (www.affymetrix.com)

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Data fields:

In the following section, the content of each field of the data files are described. Microarray probesets, for example found to be differentially expressed between different types of leukemia samples are further described by additional information.

15

The fields are of the following types:

1. GeneChip Array Information
2. Probe Design Information
3. Public Domain and Genomic References

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1. GeneChip Array Information

HG-U133 ProbeSet_ID:

25 HG-U133 ProbeSet_ID describes the probe set identifier. Examples are: 200007_at, 200011_s_at, 200012_x_at.

GeneChip:

30 The description of the GeneChip probe array name where the respective probeset is represented. Examples are: Affymetrix Human Genome U133A Array or Affymetrix Human Genome U133B Array.

2. Probe Design Information

Sequence Type:

35 The Sequence Type indicates whether the sequence is an Exemplar, Consensus or Control sequence. An Exemplar is a single nucleotide sequence taken directly from a public database. This sequence could be an mRNA or EST. A Consensus

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sequence, is a nucleotide sequence assembled by Affymetrix, based on one or more sequence taken from a public database.

Transcript ID:

5 The cluster identification number with a sub-cluster identifier appended.

Sequence Derived From:

10 The accession number of the single sequence, or representative sequence on which the probe set is based. Refer to the "Sequence Source" field to determine the database used.

Sequence ID:

15 For Exemplar sequences: Public accession number or GenBank identifier. For Consensus sequences: Affymetrix identification number or public accession number.

Sequence Source:

20 The database from which the sequence used to design this probe set was taken. Examples are: GenBank®, RefSeq, UniGene, TIGR (annotations from The Institute for Genomic Research).

3. Public Domain and Genomic References

25 Most of the data in this section come from LocusLink and UniGene databases, and are annotations of the reference sequence on which the probe set is modeled.

Gene Symbol and Title:

30 A gene symbol and a short title, when one is available. Such symbols are assigned by different organizations for different species. Affymetrix annotational data come from the UniGene record. There is no indication which species-specific databank was used, but some of the possibilities include for example HUGO: The Human Genome Organization.

MapLocation:

35 The map location describes the chromosomal location when one is available.

Unigene_Accession:

UniGene accession number and cluster type. Cluster type can be "full length" or "est", or "---" if unknown.

5 LocusLink:

This information represents the LocusLink accession number.

Full Length Ref. Sequences:

10 Indicates the references to multiple sequences in RefSeq. The field contains the ID and description for each entry, and there can be multiple entries per probeSet.

Example 3: Sample preparation, processing and data analysis**Method 1:**

15 Microarray analyses were performed utilizing the GeneChip® System (Affymetrix, Santa Clara, USA). Hybridization target preparations were performed according to recommended protocols (Affymetrix Technical Manual). In detail, at time of diagnosis, mononuclear cells were purified by Ficoll-Hypaque density centrifugation. They had been lysed immediately in RLT buffer (Qiagen, Hilden, Germany), frozen, and stored at -80°C from 1 week to 38 months. For gene expression profiling cell lysates of the leukemia samples were thawed, homogenized (QIAshredder, Qiagen), and total RNA was extracted (RNeasy Mini Kit, Qiagen). Subsequently, 5-10 µg total RNA isolated from 1 x 10⁷ cells was used as starting material for cDNA synthesis with oligo[(dT)₂₄T7promotor]₆₅ primer (cDNA Synthesis System, Roche Applied Science, Mannheim, Germany). cDNA products were purified by phenol/chlorophorm/IAA extraction (Ambion, Austin, USA) and acetate/ethanol-precipitated overnight. For detection of the hybridized target nucleic acid biotin-labeled ribonucleotides were incorporated during the following *in vitro* transcription reaction (Enzo BioArray HighYield RNA Transcript Labeling Kit, Enzo Diagnostics). After quantification by spectrophotometric measurements and 260/280 absorbance values assessment for quality control of the purified cRNA (RNeasy Mini Kit, Qiagen), 15 µg cRNA was fragmented by alkaline treatment (200 mM Tris-acetate, pH 8.2/500 mM potassium acetate/150 mM magnesium acetate) and added to the hybridization cocktail sufficient for five hybridizations on standard GeneChip microarrays (300 µl final volume). Washing and staining of the probe arrays was performed according to the

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recommended Fluidics Station protocol (EukGE-WS2v4). Affymetrix Microarray Suite software (version 5.0.1) extracted fluorescence signal intensities from each feature on the microarrays as detected by confocal laser scanning according to the manufacturer's recommendations.

5

Expression analysis quality assessment parameters included visual array inspection of the scanned image for the presence of image artifacts and correct grid alignment for the identification of distinct probe cells as well as both low 3'/5' ratio of housekeeping controls (mean: 1.90 for GAPDH) and high percentage of detection calls (mean: 46.3% present called genes). The 3' to 5' ratio of GAPDH probesets can be used to assess RNA sample and assay quality. Signal values of the 3' probe sets for GAPDH are compared to the Signal values of the corresponding 5' probe set. The ratio of the 3' probe set to the 5' probe set is generally no more than 3.0. A high 3' to 5' ratio may indicate degraded RNA or inefficient synthesis of ds cDNA or biotinylated cRNA (GeneChip® Expression Analysis Technical Manual, www.affymetrix.com). Detection calls are used to determine whether the transcript of a gene is detected (present) or undetected (absent) and were calculated using default parameters of the Microarray Analysis Suite MAS 5.0 software package.

20

Method 2:

Bone marrow (BM) aspirates are taken at the time of the initial diagnostic biopsy and remaining material is immediately lysed in RLT buffer (Qiagen), frozen and stored at -80 C until preparation for gene expression analysis. For microarray analysis the GeneChip System (Affymetrix, Santa Clara, CA, USA) is used. The targets for GeneChip analysis are prepared according to the current Expression Analysis. Briefly, frozen lysates of the leukemia samples are thawed, homogenized (QIAshredder, Qiagen) and total RNA extracted (RNeasy Mini Kit, Qiagen). Normally 10 ug total RNA isolated from 1×10^7 cells is used as starting material in the subsequent cDNA-Synthesis using Oligo-dT-T7-Promotor Primer (cDNA synthesis Kit, Roche Molecular Biochemicals). The cDNA is purified by phenol-chlorophorm extraction and precipitated with 100% Ethanol over night. For detection of the hybridized target nucleic acid biotin-labeled ribonucleotides are incorporated during the in vitro transcription reaction (Enzo® BioArray™ HighYield™ RNA Transcript Labeling Kit, ENZO). After quantification of the purified cRNA (RNeasy Mini Kit, Qiagen), 15 ug are fragmented by alkaline

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treatment (200 mM Tris-acetate, pH 8.2, 500 mM potassium acetate, 150 mM magnesium acetate) and added to the hybridization cocktail sufficient for 5 hybridizations on standard GeneChip microarrays. Before expression profiling Test3 Probe Arrays (Affymetrix) are chosen for monitoring of the integrity of the cRNA. Only labeled cRNA-cocktails which showed a ratio of the measured intensity of the 3' to the 5' end of the GAPDH gene less than 3.0 are selected for subsequent hybridization on HG-U133 probe arrays (Affymetrix). Washing and staining the Probe arrays is performed as described (siehe Affymetrix-Original-Literatur (LOCKHART und LIPSHUTZ)). The Affymetrix software (Microarray Suite, Version 4.0.1) extracted fluorescence intensities from each element on the arrays as detected by confocal laser scanning according to the manufacturers recommendations.

Table 1

One-Versus-All (OVA)

1.1 ball versus rest

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	201029_s_at	CD99	-4.39	2.44E-19	3.38E-15	-1.53	-13.74	Xp22.32
2	203373_at	SOCS2	-29.15	7.44E-20	2.49E-15	-1.38	-12.37	12q
3	201417_at		-4.81	6.37E-16	1.65E-12	-1.39	-12.21	
4	218589_at	P2RY5	-16.85	1.20E-19	2.49E-15	-1.33	-12.13	13q14
5	204798_at	MYB	-4.75	2.63E-17	1.21E-13	-1.32	-11.95	6q22-q23
6	209530_at	CACNB3	-5.23	1.26E-18	1.31E-14	-1.22	-11.32	12q13
7	218694_at	ALEX1	-7.80	5.23E-18	3.80E-14	-1.21	-11.22	Xq21.33-q22.2
8	210487_at	DNTT	-	1.28E-17	6.63E-14	-1.28	-11.17	10q23-q24
			236.66					
9	201540_at	FHL1	-9.07	5.49E-18	3.80E-14	-1.19	-11.03	Xq26
10	211031_s_at	CYLN2	-13.46	1.07E-17	6.38E-14	-1.16	-10.85	7q11.23
11	34726_at	CACNB3	-3.44	1.68E-16	6.34E-13	-1.13	-10.46	12q13
12	215537_x_at	DDAH2	-7.74	6.48E-17	2.69E-13	-1.12	-10.45	6p21.3
13	203372_s_at	SOCS2	-40.70	3.38E-16	1.00E-12	-1.18	-10.40	12q
14	207358_x_at	MACF1	-3.23	3.78E-15	7.86E-12	-1.13	-10.27	1p32-p31
15	210612_s_at	SYNJ2	-8.22	2.59E-16	8.96E-13	-1.10	-10.21	6q25.3
16	215111_s_at	TSC22	-6.23	2.83E-16	9.03E-13	-1.10	-10.18	13q14
17	212207_at	KIAA1025	-3.62	1.34E-15	3.10E-12	-1.11	-10.18	12q24.22
18	201028_s_at	CD99	-5.24	4.72E-16	1.31E-12	-1.08	-10.05	Xp22.32
19	210299_s_at	FHL1	-10.03	7.48E-16	1.83E-12	-1.09	-10.04	Xq26
20	208634_s_at	MACF1	-3.88	4.07E-15	8.06E-12	-1.06	-9.78	1p32-p31
21	226545_at		-6.34	2.47E-15	5.39E-12	-1.04	-9.72	
22	231982_at		-23.76	6.52E-15	1.23E-11	-1.05	-9.62	
23	217979_at	NET-6	-5.64	7.47E-15	1.35E-11	-1.01	-9.45	7p21.1
24	202262_x_at	DDAH2	-5.40	3.10E-14	5.15E-11	-1.03	-9.44	6p21.3
25	202519_at	MONDOA	-2.81	3.68E-14	5.88E-11	-1.03	-9.44	12q21.31
26	201416_at	SOX4	-4.62	9.88E-12	6.41E-09	-1.09	-9.43	6p22.3
27	202887_s_at	RTP801	-3.17	4.55E-14	7.00E-11	-1.01	-9.34	10pter-q26.12
28	209267_s_at	BIGM103	-3.67	9.36E-14	1.28E-10	-1.02	-9.32	4q22-q24
29	242051_at		-7.38	1.46E-14	2.52E-11	-1.00	-9.28	
30	212208_at	KIAA1025	-3.09	2.94E-13	3.36E-10	-1.02	-9.24	12q24.22
31	210298_x_at	FHL1	-21.64	8.11E-14	1.20E-10	-1.01	-9.10	Xq26
32	226869_at		-9.04	8.10E-12	5.42E-09	-1.03	-9.10	
33	212012_at		-11.98	9.58E-14	1.28E-10	-0.99	-9.03	
34	223383_at	NIN283	-6.63	3.14E-13	3.44E-10	-0.98	-8.99	16q22.3
35	224848_at		-3.97	8.51E-14	1.22E-10	-0.96	-8.94	
36	201015_s_at	JUP	-9.02	1.07E-13	1.37E-10	-0.96	-8.91	17q21
37	213541_s_at	ERG	-7.36	1.13E-13	1.38E-10	-0.96	-8.91	21q22.3
38	213056_at	KIAA1013	-4.12	1.37E-13	1.63E-10	-0.96	-8.88	3p14.1
39	214909_s_at	DDAH2	-4.88	1.09E-13	1.37E-10	-0.95	-8.85	6p21.3

40 210473_s_at	GPR125	-6.98	8.68E-13	8.01E-10	-0.96	-8.76 4p15.31
41 224847_at		-4.15	3.52E-13	3.75E-10	-0.94	-8.72
42 205349_at	GNA15	-5.84	3.20E-10	1.36E-07	-1.03	-8.71 19p13.3
43 218806_s_at	VAV3	-3.52	1.28E-12	1.08E-09	-0.95	-8.69 1p13.2
44 203688_at	PKD2	-3.27	1.22E-12	1.05E-09	-0.95	-8.69 4q21-q23
45 212481_s_at	TPM4	-2.93	3.00E-13	3.36E-10	-0.93	-8.66 19p13.1
46 204663_at	ME3	-3.87	6.54E-13	6.46E-10	-0.94	-8.65 11cen-q22.3
47 209360_s_at	RUNX1	-6.30	1.49E-12	1.22E-09	-0.94	-8.62 21q22.3
48 219506_at	FLJ23221	-3.43	1.73E-12	1.38E-09	-0.94	-8.61 1q21.2
49 212013_at	D2S448	-67.26	1.05E-12	9.45E-10	-0.97	-8.55 2pter-p25.1
50 212509_s_at		-7.94	5.80E-13	6.03E-10	-0.93	-8.55

1.2 cpre versus rest

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	218351_at	FLJ20502	-2.10	1.78E-07	0.00629584	-0.73	-6.30	4p11
2	205251_at	PER2	-1.88	6.61E-07	0.00629584	-0.71	-6.03	2q37.3
3	202759_s_at	AKAP2	-2.16	4.52E-07	0.00629584	-0.64	-5.75	9q31-q33
4	212371_at		-1.58	2.41E-06	0.00886562	-0.65	-5.56	
5	224450_s_at	AD034	-1.65	7.32E-07	0.00629584	-0.62	-5.56	6p24.3
6	212798_s_at	DKFZP564O043	-1.56	4.85E-06	0.01015201	-0.64	-5.43	7p21
7	221970_s_at	DKFZP586L0724	-1.62	8.88E-07	0.00629584	-0.59	-5.40	17q24.2
8	204742_s_at	APRIN	-2.08	5.00E-06	0.01015201	-0.63	-5.38	13q12.3
9	242292_at	MGC34827	-5.05	1.03E-06	0.00629584	-0.57	-5.28	Xq13.1
10	211709_s_at	SCGF	-2.97	5.53E-06	0.01015201	-0.60	-5.20	19q13.3
11	203476_at	TPBG	-4.87	1.72E-06	0.00847527	-0.55	-5.15	6q14-q15
12	202760_s_at	AKAP2	-2.45	5.38E-06	0.01015201	-0.58	-5.14	9q31-q33
13	226694_at	AKAP2	-2.69	9.09E-06	0.0123806	-0.60	-5.13	9q31-q33
14	213147_at	HOXA10	-6.10	1.98E-06	0.00847527	-0.55	-5.12	7p15-p14
15	232530_at		-6.15	2.07E-06	0.00847527	-0.55	-5.10	
16	202789_at		-1.99	2.76E-06	0.00891869	-0.55	-5.06	
17	224848_at		-2.14	5.19E-06	0.01015201	-0.56	-5.03	
18	231112_at	SNRPE	-2.54	3.15E-06	0.00891869	-0.54	-5.02	1q32
19	217828_at	FLJ13213	-1.40	8.90E-06	0.0123806	-0.57	-5.01	15q21.2
20	206847_s_at	HOXA7	-3.67	3.00E-06	0.00891869	-0.54	-5.01	7p15-p14
21	230493_at		-9.21	3.55E-06	0.00932758	-0.54	-4.99	
22	226546_at		-2.13	1.08E-05	0.01295565	-0.56	-4.94	
23	212440_at	RY1	-1.34	3.19E-05	0.02520438	-0.60	-4.93	2p13.1
24	220744_s_at	WDR10	-2.18	5.65E-05	0.03407617	-0.62	-4.91	3q21
25	222409_at	CORO1C	-2.23	7.34E-06	0.01136815	-0.54	-4.89	12q24.1
26	200897_s_at	KIAA0992	-8.35	5.52E-06	0.01015201	-0.53	-4.86	4q32.3
27	224839_s_at	GPT2	-6.98	5.97E-06	0.01015201	-0.54	-4.86	16q12.1
28	202268_s_at	APPBP1	-1.45	2.79E-05	0.02360312	-0.58	-4.86	16q22
29	209628_at	NXT2	-1.68	1.56E-05	0.01589894	-0.55	-4.84	Xq22.3
30	232201_at	NKD2	-2.39	6.08E-06	0.01015201	-0.52	-4.83	5p15.3
31	221965_at	MPHOSPH9	-1.48	1.16E-05	0.01328534	-0.54	-4.83	12q24.31

32	212018_s_at	DKFZP564M182	-1.52	3.33E-05	0.02520438	-0.57	-4.79	16p13.13
33	211953_s_at	KPNB3	-1.53	6.49E-05	0.03785948	-0.59	-4.77	13q32.2
34	202206_at	ARL7	-3.92	7.56E-06	0.01136815	-0.51	-4.77	2q37.2
35	202207_at	ARL7	-3.15	7.73E-06	0.01136815	-0.51	-4.77	2q37.2
36	228988_at	ZNF6	-3.96	1.09E-05	0.01295565	-0.52	-4.76	Xq13-q21.1
37	235918_x_at		-1.86	9.97E-06	0.01295565	-0.52	-4.76	
38	202602_s_at	HTATSF1	-1.62	3.47E-05	0.02548137	-0.56	-4.74	Xq26.1-q27.2
39	215947_s_at	FLJ14668	-1.45	2.99E-05	0.02440495	-0.55	-4.73	2p13.1
40	202169_s_at	AASDHPPT	-1.69	2.57E-05	0.02360312	-0.54	-4.70	11q22
41	224150_s_at	BITE	-2.08	1.07E-05	0.01295565	-0.51	-4.69	3q22-q23
42	207956_x_at	APRIN	-1.38	3.36E-05	0.02520438	-0.54	-4.66	13q12.3
43	208731_at	RAB2	-1.89	4.51E-05	0.02958461	-0.55	-4.65	8q12.1
44	213150_at	HOXA10	-15.88	1.39E-05	0.01502693	-0.51	-4.64	7p15-p14
45	204729_s_at	STX1A	-3.08	1.36E-05	0.01502693	-0.50	-4.64	7q11.23
46	209982_s_at	NRXN2	-2.74	1.49E-05	0.01560112	-0.50	-4.62	11q13
47	218535_s_at	FLJ11159	-1.78	0.00018413	0.064467	-0.61	-4.60	5q15
48	222763_s_at	FLJ11294	-1.71	5.51E-05	0.03407617	-0.54	-4.59	2q14.3
49	230570_at		-2.59	3.59E-05	0.02578182	-0.52	-4.58	
50	211758_x_at	APACD	-1.53	7.76E-05	0.04324801	-0.55	-4.57	2q11.2

1.3 cpreph versus rest

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	201874_at	MPZL1	-1.85	8.00E-12	1.50E-07	-0.85	-7.93	1q23.2
2	221080_s_at	FLJ22757	-1.75	8.97E-11	8.43E-07	-0.79	-7.41	19p13.3
3	203017_s_at	SSX2IP	-2.41	4.21E-10	2.64E-06	-0.77	-7.12	
4	227584_at		3.32	2.31E-08	3.52E-05	0.84	6.94	
5	202123_s_at	ABL1	2.13	1.07E-07	9.25E-05	0.92	6.89	9q34.1
6	218906_x_at	KLC2	-2.27	1.12E-08	2.64E-05	-0.75	-6.67	11q13.1
7	211990_at	HLA-DPA1	1.81	3.29E-09	1.52E-05	0.71	6.62	6p21.3
8	213403_at		-3.01	4.05E-09	1.52E-05	-0.70	-6.56	
9	218456_at	EEG1	-2.43	6.80E-09	2.09E-05	-0.70	-6.48	12p11
10	205055_at	ITGAE	-1.71	7.80E-09	2.09E-05	-0.69	-6.41	17p13
11	206995_x_at	SCARF1	1.98	3.66E-08	4.81E-05	0.73	6.41	17p13.3
12	210448_s_at	P2RX5	-4.26	1.48E-08	2.82E-05	-0.71	-6.40	17p13.3
13	224772_at	NAV1	3.49	2.68E-07	0.00018006	0.81	6.38	
14	205484_at	SIT	-6.76	2.44E-08	3.52E-05	-0.75	-6.36	9p13-p12
15	218084_x_at	FXDYD5	1.74	6.46E-08	6.46E-05	0.73	6.35	19q12-q13.1
16	210349_at	CAMK4	-2.45	1.50E-08	2.82E-05	-0.69	-6.32	5q21.3
17	222163_s_at	MGC5347	-1.75	2.33E-08	3.52E-05	-0.67	-6.20	15q15.1
18	209625_at	PIGH	-1.68	4.86E-08	5.37E-05	-0.69	-6.20	14q11-q24
19	223046_at	EGLN1	2.62	4.40E-07	0.00020855	0.78	6.18	1q42.1
20	210487_at	DNTT	2.61	2.14E-07	0.00015498	0.73	6.15	10q23-q24
21	212998_x_at	HLA-DQB1	3.40	9.68E-07	0.00035	0.83	6.14	6p21.3
22	204612_at	PKIA	-3.66	6.53E-08	6.46E-05	-0.69	-6.07	8q21.11
23	221896_s_at	HIG1	-1.79	3.84E-08	4.81E-05	-0.65	-6.05	3p21.32

24	214051_at	TMSNB	-2.32	4.60E-08	5.37E-05	-0.64	-6.01	Xq21.33-q22.3
25	209406_at	BAG2	-2.70	8.44E-08	7.93E-05	-0.67	-5.98	6p12.3-p11.2
26	211991_s_at	HLA-DPA1	2.81	8.29E-07	0.00031812	0.75	5.97	6p21.3
27	202600_s_at	NRIP1	2.17	4.44E-07	0.00020855	0.70	5.92	21q11.2
28	224774_s_at	NAV1	3.40	1.31E-06	0.00043961	0.76	5.90	
29	201540_at	FHL1	2.35	8.76E-07	0.00032921	0.73	5.89	Xq26
30	209604_s_at	GATA3	-4.25	1.25E-07	9.77E-05	-0.66	-5.88	10p15
31	238022_at		-3.96	1.12E-07	9.25E-05	-0.63	-5.84	
32	204975_at	EMP2	2.96	2.92E-06	0.00071267	0.82	5.83	16p13.2
33	221497_x_at	EGLN1	2.48	2.24E-06	0.0006001	0.77	5.80	1q42.1
34	36545_s_at	KIAA0542	-1.74	1.13E-07	9.25E-05	-0.62	-5.80	22q12.2
35	231887_s_at	KIAA1274	2.34	3.55E-06	0.00079396	0.83	5.80	10q22.1
36	219686_at	HSA250839	5.65	1.67E-06	0.00052132	0.74	5.79	4p16.2
37	229390_at		2.38	8.08E-07	0.00031624	0.67	5.71	
38	202732_at	PKIG	-2.07	2.25E-07	0.0001566	-0.62	-5.69	20q12-q13.1
39	217478_s_at	HLA-DMA	2.20	1.83E-06	0.00055506	0.71	5.69	6p21.3
40	205417_s_at	DAG1	-1.84	2.00E-07	0.00015005	-0.61	-5.67	3p21
41	202599_s_at	NRIP1	2.19	1.19E-06	0.00041411	0.68	5.66	21q11.2
42	205590_at	RASGRP1	-4.29	3.27E-07	0.00019207	-0.63	-5.65	15q15
43	207781_s_at	ZNF6	-4.64	2.95E-07	0.00018618	-0.62	-5.64	Xq13-q21.1
44	215699_x_at	KIAA0542	-1.79	3.07E-07	0.00018618	-0.61	-5.63	22q12.2
45	210299_s_at	FHL1	2.70	3.87E-06	0.00081637	0.75	5.62	Xq26
46	209569_x_at	D4S234E	-2.53	3.71E-07	0.00020855	-0.62	-5.59	4p16.3
47	201137_s_at	HLA-DPB1	2.30	2.30E-06	0.0006001	0.69	5.59	6p21.3
48	211828_s_at	KIAA0551	-3.63	3.05E-07	0.00018618	-0.60	-5.57	3q26.31
49	56197_at	PLSCR3	-1.35	4.23E-07	0.00020855	-0.61	-5.57	17p13.1
50	222154_s_at	DKFZP564A2416	6.69	8.29E-06	0.00126038	0.85	5.56	2q33.1

1.4 kort versus rest

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	209619_at	CD74	-10.29	1.17E-25	3.97E-21	-1.61	-15.03	5q32
2	208690_s_at	PDLIM1	-9.01	2.80E-21	4.73E-17	-1.36	-12.68	10q22-q26.3
3	217478_s_at	HLA-DMA	-8.30	2.55E-20	2.87E-16	-1.32	-12.24	6p21.3
4	211990_at	HLA-DPA1	-6.61	3.43E-19	2.90E-15	-1.33	-12.20	6p21.3
5	221581_s_at	WBSCR5	-9.74	5.40E-19	3.65E-15	-1.28	-11.75	7q11.23
6	210982_s_at	HLA-DRA	-14.97	7.49E-19	4.22E-15	-1.26	-11.59	6p21.3
7	215933_s_at	HHEX	-7.26	9.57E-19	4.63E-15	-1.24	-11.47	10q23.32
8	204689_at	HHEX	-4.92	1.00E-16	3.09E-13	-1.23	-11.15	10q23.32
9	208894_at	HLA-DRA	-12.83	9.91E-18	4.19E-14	-1.20	-11.05	6p21.3
10	226459_at	FLJ35564	-5.62	3.24E-17	1.22E-13	-1.14	-10.60	10q23.33
11	201015_s_at	JUP	-19.72	7.26E-17	2.46E-13	-1.13	-10.48	17q21
12	229597_s_at	KIAA1607	-4.84	5.73E-16	1.49E-12	-1.13	-10.35	10q11.21
13	201137_s_at	HLA-DPB1	-7.53	1.17E-16	3.29E-13	-1.11	-10.33	6p21.3
14	230917_at		-4.98	6.19E-16	1.50E-12	-1.07	-9.97	

15	224925_at	PRex1	-5.95	8.09E-16	1.83E-12	-1.07	-9.92	20q13.13
16	213539_at	CD3D	7.99	1.94E-08	3.07E-06	1.53	9.92	11q23
17	226878_at		-4.92	1.10E-15	2.34E-12	-1.06	-9.89	
18	207655_s_at	BLNK	-17.36	1.37E-15	2.74E-12	-1.07	-9.88	10q23.2-q23.33
19	206398_s_at	CD19	-18.28	6.19E-15	9.52E-12	-1.12	-9.80	16p11.2
20	211991_s_at	HLA-DPA1	-14.78	2.35E-15	4.29E-12	-1.06	-9.79	6p21.3
21	217979_at	NET-6	-6.46	2.41E-15	4.29E-12	-1.04	-9.71	7p21.1
22	241871_at		4.94	2.06E-08	3.22E-06	1.47	9.71	
23	204670_x_at	HLA-DRB5	-5.55	5.80E-15	9.35E-12	-1.04	-9.67	6p21.3
24	223553_s_at	FLJ22570	-4.05	3.26E-15	5.51E-12	-1.03	-9.60	5q35.3
25	208306_x_at	HLA-DRB4	-6.59	8.66E-15	1.22E-11	-1.04	-9.59	6p21.3
26	204249_s_at	LMO2	-6.22	7.14E-15	1.05E-11	-1.02	-9.47	11p13
27	200601_at	ACTN4	-2.87	1.38E-14	1.79E-11	-1.01	-9.36	19q13
28	226496_at	FLJ22611	-7.61	3.24E-14	3.65E-11	-1.03	-9.34	9p12
29	218029_at	FLJ13725	-5.63	1.35E-14	1.79E-11	-1.00	-9.31	16q21
30	209374_s_at	IGHM	-9.03	2.37E-14	2.97E-11	-1.01	-9.29	14q32.33
31	209312_x_at	HLA-DRB1	-5.81	4.25E-14	4.64E-11	-1.00	-9.25	6p21.3
32	224909_s_at	PRex1	-3.66	3.66E-13	2.93E-10	-1.02	-9.23	20q13.13
33	203932_at	HLA-DMB	-5.30	1.59E-13	1.54E-10	-1.01	-9.22	6p21.3
34	215193_x_at	HLA-DRB1	-7.69	2.60E-14	3.14E-11	-0.98	-9.16	6p21.3
35	225129_at	CPNE2	-4.72	3.07E-14	3.58E-11	-0.98	-9.14	16q12.2
36	205101_at	MHC2TA	-12.30	1.11E-13	1.16E-10	-1.01	-9.06	16p13
37	201536_at	DUSP3	-3.62	1.79E-13	1.68E-10	-0.98	-9.02	17q21
38	219202_at	FLJ22341	-3.84	2.51E-13	2.23E-10	-0.98	-8.99	17q25.3
39	202789_at		2.93	4.98E-08	7.02E-06	1.31	8.91	
40	212099_at		-6.73	1.13E-13	1.16E-10	-0.95	-8.87	
41	209199_s_at	MEF2C	-33.58	3.72E-13	2.93E-10	-1.01	-8.85	5q14
42	207857_at	LILRA2	-6.38	1.37E-13	1.36E-10	-0.95	-8.82	19q13.4
43	201721_s_at	LAPTM5	-2.23	2.89E-08	4.35E-06	-1.24	-8.79	1p34
44	221969_at	PAX5	-12.75	4.37E-13	3.21E-10	-0.98	-8.77	9p13
45	212827_at	IGHM	-6.45	2.38E-13	2.17E-10	-0.94	-8.72	14q32.33
46	214924_s_at	OIP106	-2.26	4.89E-10	1.38E-07	-1.05	-8.68	3p25.3-p24.1
47	227013_at	LATS2	-10.20	2.92E-13	2.53E-10	-0.93	-8.68	13q11-q12
48	202723_s_at	FOXO1A	-8.16	3.64E-13	2.93E-10	-0.94	-8.67	13q14.1
49	227077_at		3.52	4.58E-07	4.61E-05	1.57	8.65	
50	210349_at	CAMK4	3.17	2.53E-07	2.78E-05	1.42	8.63	5q21.3

1.5 pret versus rest

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	210982_s_at	HLA-DRA	-17.62	4.50E-18	1.05E-13	-1.18	-11.04	6p21.3
2	208894_at	HLA-DRA	-17.14	1.41E-17	1.65E-13	-1.18	-10.88	6p21.3
3	208306_x_at	HLA-DRB4	-7.91	5.39E-17	4.21E-13	-1.13	-10.49	6p21.3
4	209312_x_at	HLA-DRB1	-7.48	1.03E-16	6.04E-13	-1.11	-10.36	6p21.3
5	209771_x_at	CD24	-10.54	2.07E-15	5.12E-12	-1.13	-10.31	6q21

6	204670_x_at	HLA-DRB5	-6.90	3.79E-16	1.77E-12	-1.11	-10.30	6p21.3
7	217478_s_at	HLA-DMA	-6.73	1.34E-15	3.92E-12	-1.12	-10.29	6p21.3
8	215193_x_at	HLA-DRB1	-12.28	6.18E-16	2.41E-12	-1.09	-10.06	6p21.3
9	203932_at	HLA-DMB	-5.56	7.45E-16	2.49E-12	-1.08	-10.06	6p21.3
10	216379_x_at	KIAA1919	-10.22	2.19E-15	5.12E-12	-1.09	-10.03	6q22
11	202113_s_at	SNX2	-3.66	1.09E-14	1.70E-11	-1.09	-9.98	5q23
12	201137_s_at	HLA-DPB1	-9.10	8.41E-15	1.51E-11	-1.07	-9.86	6p21.3
13	211336_x_at	LILRB1	-10.71	5.46E-15	1.16E-11	-1.05	-9.62	19q13.4
14	211991_s_at	HLA-DPA1	-15.40	8.00E-15	1.51E-11	-1.01	-9.42	6p21.3
15	206398_s_at	CD19	-18.00	1.79E-14	2.46E-11	-1.04	-9.39	16p11.2
16	266_s_at	CD24	-13.56	1.03E-14	1.70E-11	-1.00	-9.36	6q21
17	226496_at	FLJ22611	-9.53	1.54E-14	2.26E-11	-1.01	-9.32	9p12
18	214390_s_at	BCAT1	-9.74	1.43E-13	1.85E-10	-0.97	-8.89	12pter-q12
19	212998_x_at	HLA-DQB1	-17.46	1.97E-13	2.35E-10	-0.94	-8.75	6p21.3
20	208650_s_at	CD24	-14.54	2.00E-13	2.35E-10	-0.93	-8.72	6q21
21	221969_at	PAX5	-15.18	4.60E-13	4.89E-10	-0.94	-8.62	9p13
22	229487_at		-9.85	4.35E-13	4.85E-10	-0.92	-8.56	
23	211990_at	HLA-DPA1	-5.84	4.66E-08	8.20E-06	-1.07	-8.47	6p21.3
24	203603_s_at	ZFXH1B	-4.36	1.10E-12	1.12E-09	-0.91	-8.46	2q22
25	202114_at	SNX2	-3.24	3.36E-12	2.81E-09	-0.92	-8.43	5q23
26	213537_at	HLA-DPA1	-14.15	1.95E-12	1.91E-09	-0.90	-8.30	6p21.3
27	221807_s_at	PP2447	-6.70	2.32E-12	2.17E-09	-0.89	-8.22	22q13.33
28	203543_s_at	BTEB1	-13.41	2.72E-12	2.45E-09	-0.89	-8.22	9q13
29	221000_s_at	FKSG28	-5.04	3.22E-12	2.79E-09	-0.87	-8.14	10q24.31
30	221879_at	MGC4809	-4.60	3.72E-12	3.00E-09	-0.87	-8.10	15q22.2
31	232204_at	EBF	-43.62	5.79E-12	4.52E-09	-0.90	-8.10	5q34
32	204446_s_at	ALOX5	-7.54	1.25E-11	9.15E-09	-0.87	-8.00	10q11.2
33	210146_x_at	LILRB2	-7.96	1.01E-11	7.63E-09	-0.86	-7.99	19q13.4
34	207697_x_at	LILRB2	-4.84	6.33E-10	2.65E-07	-0.91	-7.98	19q13.4
35	207467_x_at	CAST	-2.91	9.65E-09	2.26E-06	-0.95	-7.98	5q15-q21
36	226878_at		-3.93	4.94E-10	2.22E-07	-0.90	-7.94	
37	208651_x_at	CD24	-6.55	3.91E-10	1.79E-07	-0.88	-7.83	6q21
38	205640_at	ALDH3B1	-5.51	1.36E-11	9.63E-09	-0.84	-7.81	11q13
39	222701_s_at	MGC2217	-3.28	6.51E-09	1.77E-06	-0.90	-7.75	8q11.23
40	201161_s_at	CSDA	-4.98	3.70E-07	4.33E-05	-1.00	-7.73	12p13.1
41	227646_at		-22.93	3.36E-11	2.25E-08	-0.85	-7.70	
42	205049_s_at	CD79A	-7.16	2.78E-11	1.91E-08	-0.82	-7.66	19q13.2
43	224796_at	DDEF1	-2.01	6.93E-11	4.38E-08	-0.83	-7.64	8q24.1-q24.2
44	203300_x_at	AP1S2	-2.09	1.06E-10	6.52E-08	-0.83	-7.64	Xp22.31
45	222217_s_at	SLC27A3	-3.67	3.42E-10	1.60E-07	-0.85	-7.63	1q21.1
46	205101_at	MHC2TA	-6.89	4.66E-11	3.03E-08	-0.81	-7.58	16p13
47	226459_at	FLJ35564	-3.89	4.44E-09	1.27E-06	-0.87	-7.57	10q23.33
48	56256_at	CGI-40	-2.07	1.80E-10	9.58E-08	-0.81	-7.44	11q23.3
49	204604_at	PFTK1	-4.97	1.87E-10	9.74E-08	-0.80	-7.40	7q21-q22
50	208178_x_at	TRIO	-6.80	1.09E-10	6.52E-08	-0.80	-7.38	5p15.1-p14

1.6 prob versus rest

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	227353_at	EVER2	-3.51	1.16E-19	1.25E-15	-1.27	-11.86	17q25.3
2	225637_at	FLJ20186	-5.19	1.10E-19	1.25E-15	-1.27	-11.85	16q24.3
3	202853_s_at	RYK	-4.26	2.36E-18	1.70E-14	-1.20	-11.18	3q22
4	204949_at	ICAM3	-5.58	2.74E-17	1.47E-13	-1.18	-10.85	19p13.3- p13.2
5	225563_at	LOC255967	4.22	6.51E-10	4.52E-07	1.73	10.82	13q12.13
6	214022_s_at	MGC27165	-4.47	9.06E-17	3.90E-13	-1.11	-10.38	14
7	226496_at	FLJ22611	3.44	5.02E-11	5.15E-08	1.27	9.94	9p12
8	225314_at	MGC45416	-4.59	4.36E-15	1.34E-11	-1.08	-9.81	4p11
9	201601_x_at	MGC27165	-5.51	3.84E-15	1.34E-11	-1.07	-9.79	14
10	204069_at	MEIS1	22.75	1.51E-08	4.53E-06	1.96	9.61	2p14-p13
11	200871_s_at	PSAP	-3.42	5.75E-14	1.55E-10	-0.96	-8.99	10q21-q22
12	214172_x_at	RYK	-2.81	3.34E-13	7.63E-10	-0.95	-8.78	3q22
13	204661_at	CDW52	-8.65	3.54E-13	7.63E-10	-0.95	-8.71	1p36
14	239214_at		6.80	7.21E-08	1.46E-05	1.49	8.45	
15	228046_at	LOC152485	-6.12	1.21E-12	2.18E-09	-0.91	-8.43	4q31.1
16	34210_at	CDW52	-7.94	1.06E-12	2.08E-09	-0.91	-8.42	1p36
17	204328_at	EVER1	-2.05	6.17E-12	9.64E-09	-0.91	-8.27	17q25.3
18	212063_at	CD44	2.59	2.51E-08	6.51E-06	1.16	8.16	11p13
19	228754_at	KIAA1719	-2.75	6.03E-11	5.90E-08	-0.91	-8.09	3p24-p23
20	219463_at	C20orf103	17.73	1.28E-07	2.25E-05	1.39	8.09	20p12
21	226764_at	LOC152485	-14.04	1.40E-11	1.74E-08	-0.90	-8.02	4q31.1
22	209822_s_at	VLDLR	7.32	1.86E-07	2.85E-05	1.48	8.01	9p24
23	221969_at	PAX5	4.33	9.12E-08	1.75E-05	1.25	7.98	9p13
24	242414_at		4.39	1.33E-07	2.27E-05	1.33	7.98	
25	203020_at	KIAA0471	-2.03	6.27E-12	9.64E-09	-0.86	-7.98	1q24-q25
26	227134_at	JFC1	-2.40	1.41E-11	1.74E-08	-0.86	-7.96	1p35.3
27	203593_at	CD2AP	-4.02	1.46E-11	1.74E-08	-0.86	-7.91	6p12
28	225912_at	TP53INP1	-5.53	1.06E-11	1.52E-08	-0.84	-7.87	8q22
29	207734_at	LAX	-1.93	3.02E-11	3.42E-08	-0.85	-7.80	1q32.1
30	215925_s_at	CD72	7.99	2.65E-07	3.67E-05	1.36	7.74	9p13.1
31	218066_at	SLC12A7	1.98	1.43E-08	4.35E-06	0.97	7.65	5p15
32	203725_at	GADD45A	-3.29	3.30E-11	3.55E-08	-0.82	-7.63	1p31.2- p31.1
33	219033_at	FLJ21308	3.84	3.87E-07	5.05E-05	1.30	7.51	5q11.1
34	225703_at	KIAA1545	2.27	1.65E-07	2.64E-05	1.10	7.46	12q24.33
35	228758_at		-4.41	9.31E-11	8.72E-08	-0.80	-7.43	
36	200045_at - HG- U133B	ABCF1	-1.65	3.29E-10	2.62E-07	-0.81	-7.36	6p21.33
37	217940_s_at	FLJ10769	-2.82	1.29E-10	1.16E-07	-0.79	-7.34	13q33.3
38	203139_at	DAPK1	-4.55	1.88E-10	1.62E-07	-0.78	-7.24	9q34.1
39	228083_at	CACNA2D4	7.35	6.61E-07	7.66E-05	1.22	7.20	12p13.33
40	55872_at	KIAA1196	-3.43	3.05E-10	2.53E-07	-0.78	-7.20	20q13.33
41	204794_at	DUSP2	-3.94	3.70E-10	2.84E-07	-0.79	-7.19	2q11
42	217168_s_at	HERPUD1	-2.28	6.84E-10	4.60E-07	-0.79	-7.19	16q12.2-q13
43	219045_at	ARHF	-2.26	3.31E-09	1.45E-06	-0.81	-7.14	12q24.31

44	243618_s_at	LOC152485	-29.88	9.50E-10	5.68E-07	-0.84	-7.11	4q31.1
45	200965_s_at	ABLIM1	-4.68	4.57E-10	3.32E-07	-0.76	-7.07	10q25
46	225613_at	KIAA0303	-3.95	4.63E-10	3.32E-07	-0.76	-7.05	5q12.3
47	210024_s_at	UBE2E3	-3.55	8.10E-10	4.98E-07	-0.76	-7.01	2q32.1
48	203435_s_at	MME	-20.47	1.51E-09	7.93E-07	-0.81	-6.98	3q25.1-q25.2
49	219648_at	FLJ10116	-4.27	7.10E-10	4.63E-07	-0.75	-6.97	2q35
50	210424_s_at	GOLGIN-67	-4.01	2.66E-09	1.25E-06	-0.78	-6.97	15q11.2

Table 2

2. All-Pairs (AP)

2.1 ball versus cpre

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	219506_at	FLJ23221	-3.45	9.55E-06	0.16997203	-1.54	-6.75	1q21.2
2	235509_at	MGC40214	1.55	4.30E-06	0.15843086	1.37	6.38	8q22.1
3	205006_s_at	NMT2	-3.42	1.38E-05	0.16997203	-1.36	-6.17	10p13
4	217979_at	NET-6	-7.33	0.00018505	0.30283227	-1.46	-5.60	7p21.1
5	225927_at		2.49	2.07E-05	0.19100352	1.19	5.57	
6	239835_at	TA-KRP	2.17	5.21E-05	0.2517793	1.20	5.43	3p14
7	225606_at	LOC150819	3.84	7.49E-05	0.2517793	1.18	5.32	2q12.3
8	225557_at	AXUD1	-2.99	0.00010941	0.28818669	-1.21	-5.32	3p22
9	225455_at	STAF42	1.61	4.17E-05	0.2517793	1.13	5.29	1q23.2
10	212124_at	RAI17	-3.26	6.41E-05	0.2517793	-1.15	-5.28	10q22.3
11	221624_at	TCL6	2.44	5.38E-05	0.2517793	1.14	5.27	14q32.1
12	225570_at	SLC41A1	-2.39	0.00014923	0.29947256	-1.19	-5.19	1q32.1
13	229061_s_at	SLC25A13	2.04	0.00015302	0.29947256	1.16	5.12	7q21.3
14	212841_s_at	PPFIBP2	9.54	0.00039491	0.30409429	1.34	5.10	11p15.3
15	218312_s_at	FLJ12895	-2.95	0.000104	0.28818669	-1.12	-5.09	19q13.43
16	234107_s_at	HARS2	2.75	7.51E-05	0.2517793	1.09	5.06	20p11.23
17	203688_at	PKD2	-4.76	0.00040307	0.30409429	-1.30	-5.05	4q21-q23
18	235353_at	KIAA0746	2.66	0.00010238	0.28818669	1.10	5.05	4p15.2
19	209001_s_at	DKFZP566D193	1.76	6.89E-05	0.2517793	1.07	5.02	3q22.1
20	211031_s_at	CYLN2	-15.41	0.00051954	0.30410368	-1.34	-4.96	7q11.23
21	228153_at	LOC255488	5.56	0.00035957	0.30409429	1.18	4.92	6p22.3
22	224450_s_at	AD034	1.74	0.00019836	0.30283227	1.10	4.91	6p24.3
23	224654_at		1.57	0.0001543	0.29947256	1.07	4.88	
24	201539_s_at	FHL1	-3.36	0.00046369	0.30409429	-1.21	-4.88	Xq26
25	236656_s_at		-5.07	0.00055979	0.30521174	-1.28	-4.88	
26	221268_s_at	SGPP1	2.14	0.0002704	0.30283227	1.11	4.85	14q23.1
27	218066_at	SLC12A7	-2.31	0.00012424	0.29947256	-1.04	-4.84	5p15
28	213541_s_at	ERG	-11.53	0.00066791	0.30549286	-1.36	-4.83	21q22.3
29	210835_s_at	CTBP2	-3.11	0.00021882	0.30283227	-1.06	-4.79	10q26.2
30	203859_s_at	PALM	-3.45	0.00026474	0.30283227	-1.07	-4.76	19p13.3
31	210298_x_at	FHL1	-21.41	0.00076087	0.3277722	-1.37	-4.76	Xq26

32	226005_at		2.17	0.00030052	0.30409429	1.08	4.75
33	212313_at	MGC29816	3.25	0.00044995	0.30409429	1.13	4.74 8p21.2
34	202136_at	BS69	-2.79	0.00039144	0.30409429	-1.10	-4.73 10p14
35	220987_s_at	SNARK	1.99	0.00014577	0.29947256	1.00	4.69 1q32.1
36	201220_x_at	CTBP2	-2.67	0.00026099	0.30283227	-1.04	-4.69 10q26.2
37	203198_at	CDK9	-2.29	0.00019436	0.30283227	-1.02	-4.68 9q34.1
38	226271_at		2.75	0.00022029	0.30283227	1.02	4.68
39	203664_s_at	POLR2D	1.68	0.0002083	0.30283227	1.02	4.68 2q21
40	212012_at		-14.45	0.00086071	0.33453416	-1.33	-4.67
41	232950_s_at	NIR3	3.01	0.00048654	0.30409429	1.10	4.66 12q24.31
42	203373_at	SOCS2	-25.42	0.00091929	0.33453416	-1.36	-4.64 12q
43	228390_at		7.11	0.00073011	0.32052047	1.18	4.64
44	212136_at	ATP2B4	-2.54	0.00037147	0.30409429	-1.05	-4.64 1q25-q32
45	209048_s_at	PRKCBP1	-1.72	0.00023474	0.30283227	-1.01	-4.63 20q13.12
46	210644_s_at	LAIR1	-2.97	0.00025775	0.30283227	-1.01	-4.62 19q13.4
47	235273_at	EKN1	4.18	0.0002388	0.30283227	1.00	4.61 15q21.1
48	203622_s_at	LOC56902	1.61	0.00025645	0.30283227	0.99	4.57 2p13.2
49	215222_x_at	MACF1	-2.43	0.00048313	0.30409429	-1.05	-4.57 1p32-p31
50	242292_at	MGC34827	5.07	0.00055811	0.30521174	1.07	4.56 Xq13.1

2.2 ball versus cpreph

#	affy id	HUGO name	fc	p	q	str	t	Map Location
1	203373_at	SOCS2	-36.06	5.83E-14	1.74E-09	-3.09	-15.85	12q
2	201029_s_at	CD99	-4.72	1.47E-13	2.20E-09	-2.06	-12.13	Xp22.32
3	210487_at	DNTT	-	2.87E-11	2.87E-07	-2.41	-11.84	10q23-q24
4	201540_at	FHL1	-13.76	1.19E-10	8.91E-07	-1.98	-10.66	Xq26
5	212012_at		-19.01	1.12E-09	2.40E-06	-1.88	-9.72	
6	217979_at	NET-6	-7.66	3.59E-10	1.19E-06	-1.71	-9.65	7p21.1
7	227584_at		-6.64	6.56E-10	1.78E-06	-1.69	-9.46	
8	215537_x_at	DDAH2	-6.41	2.41E-10	9.21E-07	-1.61	-9.33	6p21.3
9	209806_at	HIST1H2BK	-3.24	1.90E-10	9.21E-07	-1.59	-9.27	6p21.33
10	203372_s_at	SOCS2	-51.95	3.20E-09	5.64E-06	-1.86	-9.25	12q
11	202123_s_at	ABL1	-3.32	5.33E-10	1.60E-06	-1.57	-9.08	9q34.1
12	213056_at	KIAA1013	-5.29	8.82E-10	2.03E-06	-1.59	-9.05	3p14.1
13	224710_at	RAB34	-6.65	2.24E-10	9.21E-07	-1.53	-9.02	17q11.1
14	210299_s_at	FHL1	-16.35	4.90E-09	7.72E-06	-1.71	-8.95	Xq26
15	204663_at	ME3	-3.67	2.46E-10	9.21E-07	-1.51	-8.95	11cen-q22.3
16	202519_at	MONDOA	-3.70	1.28E-09	2.56E-06	-1.56	-8.89	12q21.31
17	218589_at	P2RY5	-19.16	6.12E-09	8.73E-06	-1.71	-8.86	13q14
18	206995_x_at	SCARF1	-3.07	7.92E-10	1.98E-06	-1.47	-8.66	17p13.3
19	212013_at	D2S448	-	1.35E-08	1.45E-05	-1.73	-8.55	2pter-p25.1
20	219506_at	FLJ23221	-4.99	4.22E-09	7.02E-06	-1.48	-8.42	1q21.2
21	209530_at	CACNB3	-4.68	8.41E-09	1.05E-05	-1.49	-8.31	12q13
22	224772_at	NAV1	-6.79	1.23E-08	1.37E-05	-1.50	-8.26	

23	226869_at	-9.84	1.72E-09	3.22E-06	-1.39	-8.23
24	201015_s_at JUP	-13.18	1.16E-08	1.37E-05	-1.47	-8.18 17q21
25	223467_at RASD1	-24.21	3.64E-08	3.20E-05	-1.53	-7.99 17p11.2
26	201383_s_at M17S2	2.15	7.42E-08	5.29E-05	1.42	7.94 17q21.1
27	211671_s_at NR3C1	-2.87	8.11E-09	1.05E-05	-1.36	-7.92 5q31
28	211031_s_at CYLN2	-16.82	4.21E-08	3.60E-05	-1.45	-7.82 7q11.23
29	202262_x_at DDAH2	-4.66	6.10E-09	8.73E-06	-1.32	-7.79 6p21.3
30	218694_at ALEX1	-7.99	2.64E-08	2.47E-05	-1.36	-7.69 Xq21.33-q22.2
31	217870_s_at UMP-CMPK	-1.70	2.39E-08	2.44E-05	-1.32	-7.67
32	238365_s_at	-6.09	8.16E-09	1.05E-05	-1.30	-7.66
33	211709_s_at SCGF	-6.71	2.52E-08	2.44E-05	-1.33	-7.63 19q13.3
34	219686_at HSA250839	-48.82	9.91E-08	6.59E-05	-1.52	-7.61 4p16.2
35	222488_s_at DCTN4	-4.16	1.20E-08	1.37E-05	-1.29	-7.57 5q31-q32
36	202052_s_at RAI14	-10.79	9.03E-08	6.14E-05	-1.40	-7.52 5p13.3-p13.2
37	234107_s_at HARS2	4.82	6.57E-06	0.00111787	1.57	7.43 20p11.23
38	218966_at MYO5C	-4.11	4.68E-08	3.89E-05	-1.30	-7.43 15q21
39	223276_at NID67	-6.25	2.46E-08	2.44E-05	-1.27	-7.42 5q33.1
40	209691_s_at DOK4	-15.12	1.34E-07	7.82E-05	-1.42	-7.41 16q12.2
41	242051_at	-7.24	7.04E-08	5.15E-05	-1.32	-7.40
42	214505_s_at FHL1	-9.48	1.36E-07	7.82E-05	-1.36	-7.32 Xq26
43	227998_at MGC17528	-8.34	1.61E-07	8.46E-05	-1.34	-7.23
44	201865_x_at NR3C1	-2.49	2.89E-08	2.62E-05	-1.22	-7.22 5q31
45	202600_s_at NRIP1	-4.39	7.05E-08	5.15E-05	-1.24	-7.22 21q11.2
46	204798_at MYB	-4.08	5.11E-08	4.02E-05	-1.22	-7.15 6q22-q23
47	209679_s_at LOC57228	-6.69	8.71E-08	6.06E-05	-1.22	-7.06 12q13.12
48	225157_at MONDOA	-3.72	1.85E-07	9.40E-05	-1.27	-7.05 12q21.31
49	229649_at NRXN3	-8.32	1.57E-07	8.46E-05	-1.25	-7.04 14q31
50	209267_s_at BIGM103	-2.90	5.02E-08	4.02E-05	-1.19	-7.02 4q22-q24

2.3 ball versus kort

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	201029_s_at	CD99	-5.22	5.39E-12	1.98E-07	-2.91	-14.25	Xp22.32
2	201028_s_at	CD99	-6.96	1.11E-09	2.03E-05	-2.97	-13.33	Xp22.32
3	213539_at	CD3D	-15.81	3.55E-08	0.00033205	-2.77	-11.27	11q23
4	201417_at		-6.05	3.61E-08	0.00033205	-2.00	-9.42	
5	228174_at		-5.79	1.45E-07	0.00066628	-2.12	-9.40	
6	209619_at	CD74	9.54	1.08E-06	0.00196468	2.21	9.28	5q32
7	204446_s_at	ALOX5	5.72	3.79E-07	0.00126579	2.01	9.07	10q11.2
8	210094_s_at	PARD3	-18.69	6.05E-07	0.00158863	-2.00	-8.60	10p11.21
9	221526_x_at	PARD3	-8.93	4.88E-07	0.00138049	-1.75	-8.09	10p11.21
10	205006_s_at	NMT2	-7.91	1.32E-06	0.0021086	-1.81	-7.92	10p13
11	203124_s_at	SLC11A2	-2.83	7.96E-08	0.000488	-1.59	-7.90	12q13
12	228007_at		-4.37	9.84E-07	0.00196468	-1.74	-7.86	
13	228046_at	LOC152485	-3.47	8.47E-07	0.00195738	-1.70	-7.81	4q31.1

14	226048_at		-3.02	2.97E-07	0.00121315	-1.61	-7.77
15	226178_at		-1.96	7.73E-08	0.000488	-1.55	-7.73
16	201416_at	SOX4	-5.83	4.18E-07	0.00128174	-1.61	-7.71 6p22.3
17	205689_at	KIAA0435	-3.37	1.04E-07	0.00054791	-1.54	-7.68 1q42.2
18	222895_s_at	BCL11B	-9.66	1.42E-06	0.0021733	-1.70	-7.66 14q32.31
19	242051_at		-11.32	3.13E-06	0.00299902	-1.78	-7.53
20	212288_at	FNBP1	-2.79	3.72E-07	0.00126579	-1.52	-7.42 9q34
21	224861_at		-7.82	2.70E-06	0.00291768	-1.65	-7.35
22	225120_at		-3.63	2.33E-06	0.00275345	-1.62	-7.31
23	235171_at		-10.37	4.82E-06	0.00369381	-1.74	-7.28
24	209604_s_at	GATA3	-7.14	2.28E-06	0.00275345	-1.58	-7.24 10p15
25	215307_at		-4.95	2.93E-06	0.00299902	-1.61	-7.22
26	209530_at	CACNB3	-6.81	5.90E-06	0.00381431	-1.72	-7.16 12q13
27	220987_s_at	SNARK	3.32	9.24E-07	0.00196468	1.45	7.08 1q32.1
28	229838_at	NUCB2	-6.70	5.34E-06	0.00372633	-1.58	-6.97 11p15.1-p14
29	234107_s_at	HARS2	3.97	1.11E-05	0.00475432	1.58	6.95 20p11.23
30	221558_s_at	LEF1	-3.53	2.18E-06	0.00275345	-1.47	-6.95 4q23-q25
31	219696_at	FLJ20054	-3.82	5.10E-06	0.00372633	-1.55	-6.94 1q31.1
32	202625_at	LYN	7.02	2.17E-05	0.00661371	1.66	6.91 8q13
33	212293_at	Nbak2	-2.47	8.52E-07	0.00195738	-1.39	-6.87 1p12
34	227077_at		-2.76	1.12E-06	0.00196468	-1.40	-6.87
35	226459_at	FLJ35564	4.75	1.65E-05	0.00593343	1.59	6.87 10q23.33
36	236126_at		-5.22	1.04E-06	0.00196468	-1.40	-6.85
37	204798_at	MYB	-4.48	3.18E-06	0.00299902	-1.46	-6.85 6q22-q23
38	202020_s_at	LANCL1	-3.57	8.64E-06	0.00418219	-1.61	-6.84 2q33-q35
39	202208_s_at	ARL7	-6.53	4.08E-06	0.00340825	-1.48	-6.84 2q37.2
40	226548_at	LOC112868	-6.69	3.83E-06	0.00327794	-1.47	-6.81 16p12.1
41	205255_x_at	TCF7	-5.89	5.19E-06	0.00372633	-1.49	-6.80 5q31.1
42	210612_s_at	SYNJ2	-9.81	8.02E-06	0.00415246	-1.54	-6.77 6q25.3
43	201778_s_at	KIAA0494	-2.27	2.47E-06	0.00275345	-1.41	-6.76 1pter-p22.1
44	217478_s_at	HLA-DMA	6.66	3.06E-05	0.00750471	1.65	6.73 6p21.3
45	219528_s_at	BCL11B	-8.87	9.26E-06	0.00442356	-1.55	-6.73 14q32.31
46	207237_at	KCNA3	-4.25	4.21E-06	0.00344128	-1.42	-6.67 1p13.3
47	202207_at	ARL7	-4.21	1.20E-06	0.00201397	-1.34	-6.63 2q37.2
48	242414_at		-4.59	5.59E-06	0.0038101	-1.43	-6.62
49	204891_s_at	LCK	-7.63	7.02E-06	0.00398198	-1.45	-6.62 1p34.3
50	226878_at		3.59	7.59E-06	0.00415246	1.41	6.60

2.4 ball versus pret

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	204446_s_at	ALOX5	14.95	2.34E-07	0.00543998	2.71	10.74	10q11.2
2	220987_s_at	SNARK	4.74	6.98E-07	0.00810368	2.34	9.41	1q32.1
3	201029_s_at	CD99	-6.27	1.65E-05	0.02405809	-2.55	-9.15	Xp22.32
4	208998_at	UCP2	3.67	1.99E-06	0.01157944	2.25	8.84	11q13
5	201416_at	SOX4	-6.90	1.24E-05	0.02304955	-2.18	-8.42	6p22.3

42;

6	201028_s_at	CD99	-6.85	7.51E-05	0.03843037	-2.38	-7.90 Xp22.32
7	204639_at	ADA	-5.24	4.89E-05	0.0344484	-2.16	-7.81 20q12-q13.11
8	216379_x_at	KIAA1919	11.99	6.50E-06	0.02165632	1.93	7.70 6q22
9	209771_x_at	CD24	13.02	8.98E-06	0.02304955	1.89	7.49 6q21
10	209312_x_at	HLA-DRB1	6.78	1.02E-05	0.02304955	1.89	7.45 6p21.3
11	208306_x_at	HLA-DRB4	6.85	1.66E-05	0.02405809	1.82	7.13 6p21.3
12	218267_at	CINP	1.89	1.88E-06	0.01157944	1.64	7.12 14q32.33
13	216705_s_at	ADA	-4.56	1.19E-05	0.02304955	-1.71	-7.11 20q12-q13.11
14	215193_x_at	HLA-DRB1	10.70	2.83E-05	0.02611171	1.94	7.09 6p21.3
15	204670_x_at	HLA-DRB5	6.71	1.46E-05	0.02405809	1.76	7.05 6p21.3
16	208914_at	GGA2	3.10	3.76E-06	0.01748227	1.63	7.00 16p12
17	226545_at		-4.43	2.63E-05	0.02611171	-1.72	-6.97
18	201417_at		-6.42	0.000115	0.04110893	-1.94	-6.97
19	224861_at		-7.27	0.00013682	0.04816829	-1.91	-6.82
20	203932_at	HLA-DMB	5.96	3.33E-05	0.02611171	1.71	6.66 6p21.3
21	227471_at	KIAA1320	-2.22	6.52E-06	0.02165632	-1.53	-6.60 6q21
22	225120_at		-2.74	8.75E-05	0.03843037	-1.68	-6.53
23	208918_s_at	FLJ13052	4.31	3.36E-05	0.02611171	1.61	6.45 1p36.33-p36.21
24	232435_at		4.30	6.59E-05	0.03843037	1.70	6.35
25	217478_s_at	HLA-DMA	5.80	3.13E-05	0.02611171	1.55	6.34 6p21.3
26	222968_at	C6orf48	-1.70	1.04E-05	0.02304955	-1.44	-6.25 6p21.3
27	45687_at	MGC3121	-2.07	6.98E-05	0.03843037	-1.54	-6.24 16p11.2
28	210982_s_at	HLA-DRA	18.70	8.63E-05	0.03843037	1.69	6.20 6p21.3
29	40148_at	APBB2	6.45	6.86E-05	0.03843037	1.60	6.18 4p13
30	204040_at	RNF144	-4.55	2.70E-05	0.02611171	-1.46	-6.18 2p25.2
31	201137_s_at	HLA-DPB1	7.48	4.32E-05	0.03186796	1.48	6.07 6p21.3
32	200754_x_at	SFRS2	-1.54	1.29E-05	0.02304955	-1.39	-6.06 17q25.3
33	213521_at		3.20	5.32E-05	0.03546673	1.47	6.01
34	235142_at	MGC17919	-13.06	0.00048562	0.06044187	-1.80	-5.94 1p34.3
35	235353_at	KIAA0746	3.36	2.95E-05	0.02611171	1.39	5.93 4p15.2
36	235171_at		-12.30	0.00054452	0.06294406	-1.89	-5.92
37	211990_at	HLA-DPA1	5.97	2.56E-05	0.02611171	1.37	5.89 6p21.3
38	208073_x_at	TTC3	-2.69	0.00043771	0.05909535	-1.69	-5.88 21q22.2
39	202494_at	PPIE	2.25	2.24E-05	0.02611171	1.36	5.88 1p32
40	208662_s_at	TTC3	-2.62	9.83E-05	0.03955716	-1.43	-5.86 21q22.2
41	212119_at	TC10	2.36	6.15E-05	0.03760523	1.41	5.81 2p21
42	204829_s_at	FOLR2	3.16	3.20E-05	0.02611171	1.36	5.81 11q13.3-q13.5
43	208894_at	HLA-DRA	19.34	0.0001665	0.05300446	1.64	5.79 6p21.3
44	239835_at	TA-KRP	2.78	2.27E-05	0.02611171	1.32	5.77 3p14
45	235749_at	UGCGL2	6.05	8.78E-05	0.03843037	1.41	5.73 13q32.1
46	206398_s_at	CD19	14.69	0.00019821	0.05397483	1.65	5.69 16p11.2
47	208740_at	SAP18	-2.93	0.00033004	0.05564195	-1.50	-5.68 13q11
48	235199_at		-5.04	0.00037185	0.05564195	-1.51	-5.64
49	225927_at		2.93	3.37E-05	0.02611171	1.30	5.64
50	212133_at	MGC5466	1.89	3.05E-05	0.02611171	1.29	5.63 15q11.2

2.5 ball versus prob

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	225563_at	LOC255967	-9.46	8.55E-11	6.80E-07	-2.71	-12.97	13q12.13
2	203373_at	SOCS2	-46.46	1.48E-10	7.67E-07	-2.86	-12.90	12q
3	204798_at	MYB	-6.78	3.48E-12	8.30E-08	-2.40	-12.77	6q22-q23
4	212207_at	KIAA1025	-5.52	2.58E-10	8.40E-07	-2.12	-10.97	12q24.22
5	226496_at	FLJ22611	-5.53	1.73E-11	2.06E-07	-1.98	-10.83	9p12
6	224710_at	RAB34	-8.29	1.61E-10	7.67E-07	-1.91	-10.29	17q11.1
7	201417_at		-5.27	2.78E-10	8.40E-07	-1.83	-9.90	
8	204069_at	MEIS1	-25.06	1.34E-08	1.69E-05	-2.06	-9.63	2p14-p13
9	218066_at	SLC12A7	-3.39	2.82E-10	8.40E-07	-1.75	-9.58	5p15
10	242414_at		-11.92	1.11E-08	1.56E-05	-1.98	-9.57	
11	215537_x_at	DDAH2	-10.07	6.49E-09	1.14E-05	-1.90	-9.55	6p21.3
12	212481_s_at	TPM4	-4.17	6.70E-09	1.14E-05	-1.85	-9.39	19p13.1
13	225314_at	MGC45416	4.09	9.27E-07	0.00023268	2.12	9.32	4p11
14	201015_s_at	JUP	-10.08	2.39E-09	6.32E-06	-1.75	-9.29	17q21
15	203372_s_at	SOCS2	-63.76	2.81E-08	2.50E-05	-2.10	-9.27	12q
16	202887_s_at	RTP801	-4.44	6.51E-09	1.14E-05	-1.77	-9.18	10pter-q26.12
17	212509_s_at		-15.30	3.82E-08	2.94E-05	-1.90	-8.95	
18	221581_s_at	WBSCR5	-6.10	1.96E-08	2.33E-05	-1.75	-8.87	7q11.23
19	223276_at	NID67	-7.79	6.32E-09	1.14E-05	-1.66	-8.82	5q33.1
20	201540_at	FHL1	-10.21	3.70E-08	2.94E-05	-1.78	-8.75	Xq26
21	238750_at		-8.18	2.12E-08	2.37E-05	-1.71	-8.74	
22	214909_s_at	DDAH2	-6.07	2.48E-08	2.50E-05	-1.72	-8.71	6p21.3
23	225703_at	KIAA1545	-3.04	7.20E-09	1.14E-05	-1.60	-8.58	12q24.33
24	206674_at	FLT3	-32.72	9.08E-08	5.31E-05	-1.86	-8.53	13q12
25	212208_at	KIAA1025	-4.68	2.79E-08	2.50E-05	-1.66	-8.51	12q24.22
26	204446_s_at	ALOX5	6.42	9.34E-08	5.31E-05	1.65	8.49	10q11.2
27	209267_s_at	BIGM103	-5.72	3.60E-08	2.94E-05	-1.66	-8.47	4q22-q24
28	214623_at	FBXW3	-6.31	6.90E-09	1.14E-05	-1.56	-8.44	22q11
29	202853_s_at	RYK	4.01	7.88E-07	0.00021391	1.77	8.44	3q22
30	217168_s_at	HERPUD1	3.38	6.88E-07	0.00019769	1.75	8.43	16q12.2-q13
31	217979_at	NET-6	-7.13	4.25E-08	3.17E-05	-1.66	-8.42	7p21.1
32	223383_at	NIN283	-7.90	1.35E-08	1.69E-05	-1.58	-8.40	16q22.3
33	209822_s_at	VLDLR	-10.06	9.87E-08	5.47E-05	-1.74	-8.35	9p24
34	202262_x_at	DDAH2	-6.71	3.29E-08	2.80E-05	-1.58	-8.24	6p21.3
35	239214_at		-6.71	5.23E-08	3.78E-05	-1.58	-8.14	
36	216109_at		-4.87	9.93E-09	1.48E-05	-1.50	-8.14	
37	208302_at	HB-1	-4.98	9.03E-08	5.31E-05	-1.58	-8.02	5q31.3
38	228083_at	CACNA2D4	-18.61	2.14E-07	9.75E-05	-1.73	-8.01	12p13.33
39	206080_at	KIAA0450	2.53	2.79E-07	0.00011489	1.55	7.95	1p36.32
40	226668_at	FLJ36175	-3.91	2.83E-08	2.50E-05	-1.47	-7.89	2q24.2
41	224681_at	GNA12	-5.96	8.99E-08	5.31E-05	-1.52	-7.87	7p22-p21
42	209112_at	CDKN1B	-2.61	2.18E-08	2.37E-05	-1.43	-7.78	12p13.1-p12
43	211126_s_at	CSRP2	-12.76	2.92E-07	0.00011605	-1.61	-7.74	12q21.1

44	226043_at	AGS3	-5.30	7.78E-08	5.16E-05	-1.45	-7.69	9q34.3
45	231982_at		-28.40	3.73E-07	0.00013902	-1.64	-7.69	
46	210299_s_at	FHL1	-9.84	3.27E-07	0.00012585	-1.59	-7.66	Xq26
47	201029_s_at	CD99	-3.02	2.74E-08	2.50E-05	-1.40	-7.63	Xp22.32
48	219033_at	FLJ21308	-4.52	1.36E-07	6.77E-05	-1.45	-7.58	5q11.1
49	207030_s_at	CSRP2	-36.41	4.90E-07	0.00016478	-1.63	-7.56	12q21.1
50	226545_at		-7.49	2.27E-07	0.00010016	-1.49	-7.56	

2.6 cpre versus cpreph

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	211709_s_at	SCGF	-3.51	3.01E-06	0.07627489	-0.95	-5.62	19q13.3
2	202123_s_at	ABL1	-2.07	5.35E-05	0.29586631	-0.84	-4.84	9q34.1
3	205251_at	PER2	-2.07	4.44E-05	0.29586631	-0.81	-4.73	2q37.3
4	212018_s_at	DKFZP564M182	-1.57	6.23E-05	0.29586631	-0.78	-4.61	16p13.13
5	212150_at	KIAA0143	-1.85	6.24E-05	0.29586631	-0.78	-4.59	8q24.22
6	202476_s_at	TUBGCP2	1.62	7.50E-05	0.29586631	0.78	4.58	10q26.3
7	244533_at		-4.35	8.16E-05	0.29586631	-0.77	-4.51	
8	204671_s_at	ANKRD6	3.49	0.00104921	0.45984316	1.08	4.46	6q14.2-q16.1
9	212667_at	SPARC	-2.30	0.00013926	0.41324887	-0.74	-4.33	5q31.3-q32
10	202823_at	TCEB1	-1.60	0.00016153	0.41324887	-0.73	-4.29	8q13.3
11	226282_at		-4.46	0.00016287	0.41324887	-0.72	-4.26	
12	205333_s_at	RCE1	1.55	0.00051989	0.45984316	0.79	4.24	11q13
13	219550_at	RBIG1	-5.51	0.00024631	0.45984316	-0.76	-4.24	11q24.2
14	218543_s_at	FLJ22693	1.99	0.00140085	0.45984316	0.90	4.14	7q34
15	222152_at		1.95	0.00094531	0.45984316	0.73	3.94	
16	203770_s_at	STS	4.00	0.00245452	0.45984316	0.91	3.91	Xp22.32
17	201324_at	EMP1	-4.33	0.00056058	0.45984316	-0.69	-3.90	12p12.3
18	221020_s_at	MFTC	-1.62	0.00050055	0.45984316	-0.65	-3.86	8q22.3
19	211034_s_at	KIAA0614	1.49	0.00130377	0.45984316	0.72	3.83	12q24.12
20	216347_s_at	PPP1R13B	1.92	0.00170263	0.45984316	0.75	3.82	14q32.33
21	212149_at	KIAA0143	-1.68	0.00082464	0.45984316	-0.63	-3.71	8q24.22
22	209625_at	PIGH	1.58	0.00170769	0.45984316	0.69	3.70	14q11-q24
23	221888_at	FLJ20241	2.13	0.00298477	0.45984316	0.80	3.70	19p13.12
24	208731_at	RAB2	-2.07	0.0008126	0.45984316	-0.63	-3.70	8q12.1
25	214321_at	NOV	-6.40	0.00114004	0.45984316	-0.69	-3.69	8q24.1
26	207914_x_at	EVX1	2.48	0.0034253	0.45984316	0.83	3.68	7p15-p14
27	209924_at	CCL18	-2.70	0.00099148	0.45984316	-0.64	-3.67	17q11.2
28	213681_at	CYHR1	1.64	0.00203082	0.45984316	0.70	3.67	
29	231887_s_at	KIAA1274	-1.72	0.00086604	0.45984316	-0.62	-3.66	10q22.1
30	201636_at	FXR1	-1.52	0.00096539	0.45984316	-0.62	-3.66	3q28
31	201325_s_at	EMP1	-3.80	0.0012208	0.45984316	-0.62	-3.58	12p12.3
32	219207_at	FLJ21128	1.91	0.00272046	0.45984316	0.70	3.58	15q22.33
33	217948_at	DKFZP564B147	3.74	0.00440395	0.45984316	0.84	3.58	Xq26.3
34	206133_at	HSXIAPAF1	2.14	0.00289333	0.45984316	0.69	3.55	17p13.2
35	214615_at	P2RY10	2.57	0.00444299	0.45984316	0.81	3.55	Xq21.1

36	227792_at		-2.46	0.00127255	0.45984316	-0.60	-3.54	
37	212440_at	RY1	-1.29	0.00127528	0.45984316	-0.60	-3.53	2p13.1
38	202853_s_at	RYK	-1.69	0.00144608	0.45984316	-0.60	-3.51	3q22
39	218184_at	TUSP	1.80	0.00340796	0.45984316	0.70	3.51	6q25-q26
40	207917_at	LOC51055	-1.61	0.0014795	0.45984316	-0.60	-3.50	6
41	201247_at	SREBF2	1.63	0.00219049	0.45984316	0.63	3.49	22q13
42	213259_s_at	SARM	-2.06	0.00148403	0.45984316	-0.59	-3.48	
43	203570_at	LOXL1	-6.22	0.00190834	0.45984316	-0.65	-3.48	15q22
44	213484_at		2.77	0.00538028	0.45984316	0.81	3.46	
45	200937_s_at	RPL5	-1.15	0.00284976	0.45984316	-0.64	-3.44	1p22.1
46	200691_s_at	HSPA9B	-1.39	0.00165041	0.45984316	-0.58	-3.44	5q31.1
47	202881_x_at	RARG-1	2.79	0.00487181	0.45984316	0.74	3.44	6p23
48	208151_x_at	DDX17	1.97	0.00454937	0.45984316	0.72	3.43	22q13.1
49	202599_s_at	NRIP1	-1.89	0.0027157	0.45984316	-0.61	-3.40	21q11.2
50	219339_s_at	Eu-HMTase1	1.98	0.00480399	0.45984316	0.70	3.39	9q34.3

2.7 cpre versus kort

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	213539_at	CD3D	-14.88	1.85E-08	0.00027199	-2.45	-10.92	11q23
2	202789_at		-4.17	1.50E-08	0.00027199	-2.32	-10.64	
3	201721_s_at	LAPTM5	2.55	3.34E-09	0.00014755	1.85	9.24	1p34
4	202207_at	ARL7	-8.67	2.67E-07	0.00193624	-2.10	-9.11	2q37.2
5	241871_at		-4.47	2.70E-08	0.00029828	-1.71	-8.46	
6	209619_at	CD74	14.56	5.83E-06	0.00677701	2.18	8.37	5q32
7	211990_at	HLA-DPA1	8.36	3.01E-06	0.00505647	1.95	8.27	6p21.3
8	228174_at		-3.70	5.46E-07	0.00241163	-1.78	-8.13	
9	217478_s_at	HLA-DMA	9.98	8.71E-06	0.00795942	2.03	7.95	6p21.3
10	235737_at	TSLP	-9.55	1.87E-06	0.00480861	-1.81	-7.80	5q21.3
11	229597_s_at	KIAA1607	4.87	1.96E-06	0.00480861	1.71	7.77	10q11.21
12	242292_at	MGC34827	-13.96	2.57E-06	0.00488866	-1.77	-7.60	Xq13.1
13	215307_at		-5.27	2.77E-06	0.00488866	-1.69	-7.43	
14	202206_at	ARL7	-12.08	4.57E-06	0.00578586	-1.79	-7.37	2q37.2
15	210349_at	CAMK4	-3.06	2.63E-07	0.00193624	-1.47	-7.31	5q21.3
16	229029_at		-6.35	6.85E-07	0.00252137	-1.51	-7.29	
17	225479_at		-3.25	5.44E-07	0.00241163	-1.48	-7.25	
18	227077_at		-3.31	3.60E-07	0.00198848	-1.46	-7.22	
19	226321_at	LOC116068	-2.62	1.51E-06	0.00444235	-1.48	-7.12	5q14.3
20	218351_at	FLJ20502	-2.98	1.15E-06	0.00363025	-1.48	-7.12	4p11
21	232950_s_at	NIR3	-2.56	3.07E-07	0.00193624	-1.42	-7.11	12q24.31
22	226459_at	FLJ35564	5.32	1.48E-05	0.01038846	1.68	7.09	10q23.33
23	209771_x_at	CD24	5.30	8.40E-06	0.00795942	1.58	7.05	6q21
24	226548_at	LOC112868	-7.44	3.33E-06	0.00505647	-1.53	-7.02	16p12.1
25	225591_at	FBXO25	-2.31	1.05E-06	0.00357921	-1.43	-6.97	8p23.3
26	225286_at		4.50	7.40E-06	0.00795942	1.53	6.94	
27	202208_s_at	ARL7	-6.54	4.41E-06	0.00578586	-1.53	-6.93	2q37.2

28	210982_s_at	HLA-DRA	21.20	3.75E-05	0.01589274	1.86	6.90	6p21.3
29	222895_s_at	BCL11B	-6.34	2.32E-06	0.00488866	-1.45	-6.88	14q32.31
30	244189_at		-2.57	6.71E-07	0.00252137	-1.36	-6.78	
31	204891_s_at	LCK	-8.77	5.75E-06	0.00677701	-1.50	-6.78	1p34.3
32	226694_at	AKAP2	-5.43	4.59E-06	0.00578586	-1.44	-6.70	9q31-q33
33	216379_x_at	KIAA1919	6.13	2.39E-05	0.01281202	1.55	6.64	6q22
34	205504_at	BTK	4.92	2.76E-06	0.00488866	1.36	6.62	Xq21.33-q22
35	224593_at	DKFZp761B128	-2.29	3.27E-06	0.00505647	-1.38	-6.61	12q24.31
36	209760_at	KIAA0922	-2.27	2.41E-06	0.00488866	-1.36	-6.59	4q31.3
37	225796_at		2.72	1.40E-05	0.00993453	1.44	6.54	
38	226546_at		-3.79	6.51E-06	0.00736867	-1.40	-6.51	
39	204670_x_at	HLA-DRB5	7.74	4.26E-05	0.01619746	1.58	6.48	6p21.3
40	228007_at		-3.36	2.55E-06	0.00488866	-1.32	-6.46	
41	219528_s_at	BCL11B	-7.37	1.11E-05	0.00850103	-1.44	-6.45	14q32.31
42	219202_at	FLJ22341	5.18	4.02E-05	0.01589274	1.52	6.39	17q25.3
43	206804_at	CD3G	-14.98	2.01E-05	0.01168972	-1.53	-6.38	11q23
44	241734_at	FLJ25286	-2.81	1.91E-06	0.00480861	-1.28	-6.37	5q23.1
45	204612_at	PKIA	-5.63	1.07E-05	0.00850103	-1.38	-6.34	8q21.11
46	206314_at	ZFP	-4.88	3.85E-06	0.00531467	-1.30	-6.33	3p22.3-p21.1
47	266_s_at	CD24	6.31	4.96E-05	0.0169742	1.50	6.28	6q21
48	202557_at	STCH	-3.15	1.12E-05	0.00850103	-1.36	-6.27	21q11
49	235721_at		-5.30	8.02E-06	0.00795942	-1.33	-6.27	
50	238695_s_at	RAB39B	-4.12	3.13E-06	0.00505647	-1.26	-6.25	

2.8 cpre versus pret

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	209771_x_at	CD24	14.40	3.05E-06	0.04790095	2.10	8.35	6q21
2	217478_s_at	HLA-DMA	8.69	7.98E-06	0.04823332	1.95	7.67	6p21.3
3	216379_x_at	KIAA1919	14.88	1.10E-05	0.04923153	1.96	7.57	6q22
4	211990_at	HLA-DPA1	7.91	1.88E-06	0.04790095	1.77	7.54	6p21.3
5	202113_s_at	SNX2	3.87	7.62E-06	0.04823332	1.80	7.34	5q23
6	266_s_at	CD24	17.86	2.13E-05	0.07442246	1.91	7.18	6q21
7	210982_s_at	HLA-DRA	26.83	3.45E-05	0.08508103	1.94	6.97	6p21.3
8	204670_x_at	HLA-DRB5	10.22	3.52E-05	0.08508103	1.81	6.80	6p21.3
9	208306_x_at	HLA-DRB4	9.98	5.28E-05	0.10362628	1.77	6.55	6p21.3
10	209619_at	CD74	6.21	8.10E-06	0.04823332	1.50	6.45	5q32
11	201137_s_at	HLA-DPB1	12.99	6.54E-05	0.11029051	1.64	6.27	6p21.3
12	201161_s_at	CSDA	6.18	1.53E-05	0.06014434	1.46	6.25	12p13.1
13	213293_s_at	TRIM22	2.45	9.21E-06	0.04823332	1.43	6.24	11p15
14	208894_at	HLA-DRA	24.85	0.00010573	0.12304972	1.76	6.14	6p21.3
15	203932_at	HLA-DMB	8.59	0.00010149	0.12304972	1.65	6.07	6p21.3
16	226459_at	FLJ35564	3.96	2.67E-05	0.08393232	1.40	5.95	10q23.33
17	208651_x_at	CD24	9.40	7.60E-05	0.11948472	1.49	5.93	6q21
18	204446_s_at	ALOX5	13.16	0.00011774	0.12332854	1.58	5.91	10q11.2

19	205088_at	CXorf6	2.94	3.09E-05	0.08508103	1.38	5.89 Xq28	
20	204639_at	ADA	-2.82	0.00015852	0.13388836	-1.48	-5.87 20q12-q13.11	
21	213142_x_at	LOC54103	5.86	0.00011393	0.12332854	1.52	5.84 7q11.23	
22	209312_x_at	HLA-DRB1	10.87	0.00019668	0.13783906	1.56	5.63 6p21.3	
23	219202_at	FLJ22341	4.23	5.74E-05	0.10603287	1.32	5.61 17q25.3	
24	232594_at		2.67	4.90E-05	0.10265345	1.31	5.61	
25	221969_at	PAX5	14.49	0.00021367	0.14256177	1.57	5.60 9p13	
26	205504_at	BTB	2.84	4.73E-05	0.10265345	1.27	5.50 Xq21.33-q22	
27	211991_s_at	HLA-DPA1	21.40	0.00025046	0.1513475	1.53	5.48 6p21.3	
28	213539_at	CD3D	-11.72	0.00078516	0.21686687	-1.64	-5.46 11q23	
29	215193_x_at	HLA-DRB1	17.00	0.00027739	0.16085873	1.57	5.44 6p21.3	
30	211065_x_at	PFKL	2.50	9.23E-05	0.12304972	1.29	5.42 21q22.3	
31	203721_s_at	CGI-48	-1.54	6.67E-05	0.11029051	-1.25	-5.39 17q21.33	
32	212998_x_at	HLA-DQB1	23.06	0.00029381	0.16085873	1.50	5.37 6p21.3	
33	222915_s_at	BANK	2.85	0.00017388	0.13388836	1.33	5.36 4q23	
34	201721_s_at	LAPTM5	1.71	0.00013123	0.12886013	1.27	5.35 1p34	
35	233358_at	FLJ14311	2.00	8.82E-05	0.12304972	1.25	5.33	19
36	236745_at	FLJ34512	4.84	9.62E-05	0.12304972	1.25	5.31 16p13.3	
37	242292_at	MGC34827	-6.28	0.0005803	0.2003799	-1.42	-5.30 Xq13.1	
38	216705_s_at	ADA	-2.44	0.00016535	0.13388836	-1.24	-5.22 20q12-q13.11	
39	201160_s_at	CSDA	3.16	0.00021777	0.14256177	1.25	5.18 12p13.1	
40	210844_x_at	CTNNA1	5.22	0.00010021	0.12304972	1.20	5.16 5q31	
41	221978_at	HLA-F	2.55	0.00016221	0.13388836	1.23	5.13 6p21.3	
42	236656_s_at		6.98	0.00031739	0.16085873	1.31	5.12	
43	211004_s_at	ALDH3B1	1.99	0.00012246	0.12413388	1.18	5.08 11q13	
44	206662_at	GLRX	3.21	0.00010258	0.12304972	1.16	5.05 5q14	
45	222292_at	TNFRSF5	7.66	0.00029289	0.16085873	1.26	5.05 20q12-q13.2	
46	202699_s_at	KIAA0792	2.56	0.00019823	0.13783906	1.21	5.04 1q42.13	
47	232095_at		6.28	0.0001747	0.13388836	1.18	5.01	
48	228220_at	LOC115548	4.21	0.00035438	0.17265105	1.27	5.01 5q13.1	
49	226646_at	KLF2	2.63	0.00011379	0.12332854	1.14	4.98 19p13.13-p13.11	
50	220744_s_at	WDR10	-2.84	0.00031279	0.16085873	-1.20	-4.98 3q21	

2.9 cpre versus prob

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	225563_at	LOC255967	-4.01	4.07E-10	1.22E-05	-1.81	-9.77	13q12.13
2	204069_at	MEIS1	-19.17	1.33E-08	0.00013226	-1.93	-9.40	2p14-p13
3	242414_at		-5.64	4.25E-08	0.00031756	-1.64	-8.37	
4	212063_at	CD44	-2.87	1.18E-08	0.00013226	-1.51	-8.17	11p13
5	208302_at	HB-1	-3.77	3.01E-07	0.00151017	-1.33	-7.07	5q31.3
6	204674_at	LRMP	-3.36	6.49E-07	0.00188309	-1.37	-7.00	12p12.1
7	201153_s_at	MBNL1	-1.65	3.03E-07	0.00151017	-1.31	-6.99	3q25
8	35974_at	LRMP	-3.51	9.53E-07	0.00219068	-1.34	-6.83	12p12.1

9	239214_at		-4.06	3.80E-07	0.00162445	-1.27	-6.83
10	219033_at	FLJ21308	-3.60	4.68E-07	0.0017479	-1.28	-6.81 5q11.1
11	204044_at	QPRT	-6.38	1.66E-06	0.00300289	-1.37	-6.76 16p12.1
12	218847_at	IMP-2	-6.54	6.93E-07	0.00188309	-1.28	-6.73 3q28
13	215925_s_at	CD72	-5.40	6.19E-07	0.00188309	-1.27	-6.73 9p13.1
14	201105_at	LGALS1	-10.23	1.91E-06	0.00300289	-1.29	-6.54 22q13.1
15	242172_at		-6.31	1.82E-06	0.00300289	-1.27	-6.52
16	209822_s_at	VLDLR	-4.50	7.57E-07	0.00188632	-1.21	-6.52 9p24
17	232530_at		-15.62	3.74E-06	0.00520412	-1.36	-6.46
18	205821_at	D12S2489E	-4.97	1.29E-06	0.00275807	-1.19	-6.37 12p13.2-p12.3
19	232231_at		-6.16	1.61E-06	0.00300289	-1.20	-6.35
20	209982_s_at	NRXN2	-5.81	3.83E-06	0.00520412	-1.26	-6.30 11q13
21	203476_at	TPBG	-8.73	5.81E-06	0.00665584	-1.28	-6.20 6q14-q15
22	228580_at	HTRA3	-5.21	4.09E-06	0.00531262	-1.22	-6.20 4p16.1
23	214651_s_at	HOXA9	-49.38	8.03E-06	0.0074049	-1.36	-6.16 7p15-p14
24	219463_at	C20orf103	-8.71	1.90E-06	0.00300289	-1.10	-6.00 20p12
25	204304_s_at	PROML1	-8.91	7.57E-06	0.00731757	-1.18	-5.95 4p15.33
26	222699_s_at	FLJ13187	2.10	1.19E-05	0.00914002	1.15	5.92 8q22.1
27	207030_s_at	CSRP2	-5.17	5.59E-06	0.00665584	-1.12	-5.88 12q21.1
28	232201_at	NKD2	-3.56	1.07E-05	0.00867437	-1.15	-5.79 5p15.3
29	213147_at	HOXA10	-14.90	1.64E-05	0.01104745	-1.24	-5.78 7p15-p14
30	238750_at		-3.27	3.38E-06	0.00505227	-1.05	-5.77
31	212526_at	SPG20	-5.68	6.14E-06	0.00665584	-1.07	-5.73 13q13.1
32	237439_at	FLJ30626	-3.03	7.13E-06	0.00731757	-1.08	-5.71 17p13.1
33	222812_s_at	ARHF	2.02	9.59E-06	0.00796582	1.07	5.68 12q24.31
34	211126_s_at	CSRP2	-3.72	7.59E-06	0.00731757	-1.06	-5.66 12q21.1
35	218535_s_at	FLJ11159	-2.25	5.25E-06	0.00653825	-1.03	-5.63 5q15
36	228855_at		-4.78	1.85E-05	0.01150869	-1.12	-5.59
37	240581_at		-4.44	6.23E-06	0.00665584	-1.02	-5.56
38	232298_at		-5.21	8.29E-06	0.0074049	-1.02	-5.52
39	213150_at	HOXA10	-44.22	3.19E-05	0.01671744	-1.21	-5.49 7p15-p14
40	223475_at	LOC83690	-6.81	2.35E-05	0.01406642	-1.09	-5.47 8q13.3
41	230441_at	KIAA1909	3.52	0.00016116	0.03651205	1.25	5.46 5p15.33
42	241394_at		-3.50	8.73E-06	0.00745405	-1.00	-5.45
43	213894_at	KIAA0960	-4.48	8.42E-06	0.0074049	-1.00	-5.45 7p21.3
44	212856_at	KIAA0767	-2.76	1.66E-05	0.01104745	-1.02	-5.39 22q13.31
45	235753_at		-7.26	3.73E-05	0.01860589	-1.11	-5.36
46	228083_at	CACNA2D4	-4.72	1.13E-05	0.00888438	-0.97	-5.33 12p13.33
47	201151_s_at	MBNL1	-1.90	1.72E-05	0.0111503	-1.00	-5.32 3q25
48	209905_at	HOXA9	-	5.08E-05	0.02175935	-1.20	-5.28 7p15-p14
			142.96				
49	241985_at	FLJ37870	3.59	7.40E-05	0.02572554	1.05	5.28 5q13.3
50	233500_x_at	LLT1	-3.00	1.44E-05	0.01051093	-0.97	-5.27 12p13

2.10 cpreph versus kort

#	affy id	HUGO name	fc	p	q	stn	t	Map
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							Location
1	211990_at	HLA-DPA1	8.45	2.33E-19	5.27E-15	2.87	17.72 6p21.3
2	209619_at	CD74	12.48	1.48E-16	1.68E-12	2.84	16.79 5q32
3	213539_at	CD3D	-32.38	2.65E-08	1.11E-05	-2.94	-11.71 11q23
4	208690_s_at	PDLIM1	10.92	3.28E-12	2.48E-08	2.01	11.70 10q22-q26.3
5	215933_s_at	HHEX	8.73	1.22E-11	6.91E-08	2.04	11.51 10q23.32
6	241871_at		-10.32	5.94E-09	4.18E-06	-2.21	-11.22
7	210982_s_at	HLA-DRA	20.71	4.54E-11	2.06E-07	2.03	11.13 6p21.3
8	227584_at		13.39	2.08E-10	3.69E-07	2.05	10.62
9	217478_s_at	HLA-DMA	11.76	1.23E-10	3.49E-07	1.91	10.56 6p21.3
10	208894_at	HLA-DRA	17.95	1.81E-10	3.69E-07	1.93	10.48 6p21.3
11	218029_at	FLJ13725	6.85	7.49E-11	2.83E-07	1.77	10.24 16q21
12	210349_at	CAMK4	-4.82	5.62E-08	1.96E-05	-2.14	-10.18 5q21.3
13	201137_s_at	HLA-DPB1	10.97	2.81E-10	4.25E-07	1.73	9.83 6p21.3
14	211991_s_at	HLA-DPA1	23.54	6.66E-10	9.44E-07	1.80	9.80 6p21.3
15	204670_x_at	HLA-DRB5	7.70	1.22E-10	3.49E-07	1.65	9.74 6p21.3
16	217979_at	NET-6	8.46	2.11E-10	3.69E-07	1.64	9.62 7p21.1
17	202789_at		-3.43	1.96E-08	9.25E-06	-1.79	-9.59
18	204689_at	HHEX	5.78	1.39E-10	3.51E-07	1.56	9.39 10q23.32
19	203708_at	PDE4B	8.45	2.80E-10	4.25E-07	1.57	9.30 1p31
20	229390_at		7.33	1.55E-10	3.51E-07	1.51	9.16
21	208306_x_at	HLA-DRB4	9.66	1.25E-09	1.46E-06	1.53	8.92 6p21.3
22	209312_x_at	HLA-DRB1	8.00	1.09E-09	1.37E-06	1.50	8.85 6p21.3
23	227077_at		-4.13	1.20E-07	3.10E-05	-1.70	-8.81
24	224925_at	PRex1	8.89	4.29E-09	3.47E-06	1.59	8.81 20q13.13
25	221969_at	PAX5	7.71	3.90E-09	3.28E-06	1.57	8.77 9p13
26	212998_x_at	HLA-DQB1	22.57	5.40E-09	3.95E-06	1.60	8.76 6p21.3
27	201015_s_at	JUP	27.52	6.09E-09	4.18E-06	1.58	8.67 17q21
28	202207_at	ARL7	-6.81	2.80E-07	5.46E-05	-1.71	-8.59 2q37.2
29	201721_s_at	LAPTM5	2.32	5.06E-09	3.95E-06	1.44	8.51 1p34
30	224774_s_at	NAV1	13.55	1.39E-08	7.33E-06	1.61	8.46
31	209771_x_at	CD24	5.38	1.29E-09	1.46E-06	1.40	8.44 6q21
32	224772_at	NAV1	9.61	3.77E-09	3.28E-06	1.44	8.42
33	215193_x_at	HLA-DRB1	11.61	9.51E-09	5.53E-06	1.49	8.36 6p21.3
34	229029_at		-11.30	2.89E-07	5.56E-05	-1.61	-8.32
35	222895_s_at	BCL11B	-16.00	1.31E-06	0.00016349	-1.96	-8.29 14q32.31
36	216379_x_at	KIAA1919	5.86	2.68E-09	2.64E-06	1.39	8.28 6q22
37	221581_s_at	WBSCR5	9.93	1.70E-08	8.39E-06	1.52	8.26 7q11.23
38	224909_s_at	PRex1	4.66	3.13E-09	2.84E-06	1.37	8.21 20q13.13
39	224710_at	RAB34	5.39	9.57E-10	1.28E-06	1.33	8.21 17q11.1
40	213082_s_at	SQV7L	6.07	3.06E-09	2.84E-06	1.36	8.19 9q22.31
41	209760_at	KIAA0922	-2.96	2.14E-07	4.67E-05	-1.52	-8.15 4q31.3
42	209732_at	CLECSF2	3.03	1.60E-09	1.72E-06	1.31	8.07 12p13-p12
43	225129_at	CPNE2	6.31	1.96E-08	9.25E-06	1.45	8.07 16q12.2
44	203932_at	HLA-DMB	6.70	5.23E-09	3.95E-06	1.35	8.06 6p21.3
45	213817_at		8.87	7.46E-09	4.75E-06	1.34	7.96
46	201161_s_at	CSDA	3.47	2.43E-09	2.51E-06	1.29	7.93 12p13.1
47	223380_s_at	LATS2	5.21	1.22E-08	6.75E-06	1.35	7.92 13q11-q12

48 226459_at	FLJ35564	4.53	9.18E-09	5.48E-06	1.33	7.88 10q23.33
49 226878_at		6.64	2.44E-08	1.09E-05	1.38	7.86
50 37384_at	PPM1F	3.92	3.58E-08	1.40E-05	1.42	7.85 22q11.22

2.11 cpreph versus pret

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	211990_at	HLA-DPA1	7.99	1.27E-09	2.26E-06	2.52	13.01	6p21.3
2	210982_s_at	HLA-DRA	26.21	3.82E-11	6.71E-07	2.12	11.26	6p21.3
3	208894_at	HLA-DRA	25.74	1.49E-10	6.71E-07	2.07	10.73	6p21.3
4	204670_x_at	HLA-DRB5	10.16	8.84E-11	6.71E-07	1.90	10.39	6p21.3
5	217478_s_at	HLA-DMA	10.24	1.21E-10	6.71E-07	1.85	10.17	6p21.3
6	209771_x_at	CD24	14.60	9.03E-11	6.71E-07	1.82	10.10	6q21
7	201137_s_at	HLA-DPB1	14.15	1.76E-10	6.71E-07	1.81	9.96	6p21.3
8	211991_s_at	HLA-DPA1	26.38	6.35E-10	1.62E-06	1.87	9.87	6p21.3
9	216379_x_at	KIAA1919	14.23	3.21E-10	1.05E-06	1.75	9.66	6q22
10	227584_at		7.36	5.02E-10	1.44E-06	1.77	9.65	
11	209312_x_at	HLA-DRB1	10.95	8.13E-10	1.86E-06	1.79	9.59	6p21.3
12	208306_x_at	HLA-DRB4	12.34	1.20E-09	2.26E-06	1.79	9.48	6p21.3
13	221000_s_at	FKSG28	7.72	1.28E-09	2.26E-06	1.71	9.25	10q24.31
14	221969_at	PAX5	9.85	2.08E-09	3.34E-06	1.66	9.01	9p13
15	212998_x_at	HLA-DQB1	32.62	4.69E-09	6.03E-06	1.73	8.96	6p21.3
16	215193_x_at	HLA-DRB1	19.74	6.16E-09	7.05E-06	1.74	8.88	6p21.3
17	201161_s_at	CSDA	6.72	2.19E-09	3.34E-06	1.57	8.81	12p13.1
18	203932_at	HLA-DMB	7.47	4.75E-09	6.03E-06	1.59	8.64	6p21.3
19	229487_at		11.49	5.46E-09	6.57E-06	1.59	8.62	
20	224772_at	NAV1	8.13	8.04E-09	8.75E-06	1.61	8.57	
21	202113_s_at	SNX2	4.79	3.75E-09	5.37E-06	1.55	8.57	5q23
22	209619_at	CD74	5.32	1.13E-06	0.0003501	1.69	8.48	5q32
23	224774_s_at	NAV1	11.56	1.68E-08	1.60E-05	1.58	8.30	
24	266_s_at	CD24	19.99	1.44E-08	1.49E-05	1.55	8.28	6q21
25	211336_x_at	LILRB1	9.21	3.41E-08	3.12E-05	1.55	8.03	19q13.4
26	208650_s_at	CD24	23.01	4.41E-08	3.80E-05	1.48	7.83	6q21
27	208651_x_at	CD24	8.91	1.50E-08	1.49E-05	1.38	7.75	6q21
28	227998_at	MGC17528	13.10	7.90E-08	5.47E-05	1.52	7.70	
29	213537_at	HLA-DPA1	26.48	8.75E-08	5.72E-05	1.50	7.64	6p21.3
30	219686_at	HSA250839	41.30	1.04E-07	6.26E-05	1.49	7.57	4p16.2
31	226878_at		5.66	4.81E-08	3.80E-05	1.33	7.39	
32	203543_s_at	BTEB1	23.84	1.53E-07	8.76E-05	1.45	7.39	9q13
33	203603_s_at	ZFHX1B	4.20	4.72E-08	3.80E-05	1.32	7.36	2q22
34	223046_at	EGLN1	6.14	7.68E-08	5.47E-05	1.31	7.33	1q42.1
35	200696_s_at	GSN	6.09	4.54E-08	3.80E-05	1.29	7.27	9q33
36	202114_at	SNX2	4.22	9.43E-08	5.99E-05	1.32	7.26	5q23
37	209238_at	STX3A	3.63	6.89E-08	5.26E-05	1.30	7.26	11q12.1
38	207697_x_at	LILRB2	4.60	7.12E-08	5.26E-05	1.28	7.21	19q13.4
39	219271_at	GalNac-T10	8.35	9.77E-08	6.04E-05	1.30	7.18	2p23.1

40	221039_s_at	DDEF1	2.73	8.61E-08	5.72E-05	1.28	7.15 8q24.1-q24.2
41	203542_s_at	BTEB1	10.17	3.24E-07	0.00014823	1.38	7.05 9q13
42	223228_at	DKFZp761O17121	-3.53	0.0001022	0.00753969	-1.72	-7.00 22q13.31
43	201160_s_at	CSDA	3.67	4.85E-05	0.00452469	1.55	6.96 12p13.1
44	213521_at		3.71	1.91E-07	0.0001068	1.25	6.91
45	210146_x_at	LILRB2	7.39	1.43E-07	8.40E-05	1.23	6.90 19q13.4
46	206398_s_at	CD19	25.06	5.09E-07	0.00019422	1.38	6.88 16p11.2
47	201005_at	CD9	26.04	5.24E-07	0.00019648	1.34	6.85 12p13.3
48	209307_at	SWAP70	4.12	3.45E-07	0.00015478	1.26	6.83 11p15
49	224796_at	DDEF1	2.58	3.17E-07	0.00014791	1.25	6.82 8q24.1-q24.2
50	205101_at	MHC2TA	10.93	4.07E-07	0.00016979	1.27	6.82 16p13

2.12 cpreph versus prob

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	204069_at	MEIS1	-37.94	1.19E-08	2.37E-05	-2.18	-9.80	2p14-p13
2	34210_at	CDW52	9.83	2.02E-10	1.94E-06	1.59	9.63	1p36
3	201874_at	MPZL1	-2.35	1.26E-09	5.54E-06	-1.64	-9.59	1q23.2
4	227353_at	EVER2	3.39	8.63E-11	1.65E-06	1.51	9.46	17q25.3
5	225563_at	LOC255967	-3.50	5.63E-10	3.60E-06	-1.50	-9.21	13q12.13
6	204661_at	CDW52	10.09	1.74E-09	5.54E-06	1.51	8.91	1p36
7	225637_at	FLJ20186	5.11	1.70E-09	5.54E-06	1.43	8.66	16q24.3
8	219463_at	C20orf103	-37.27	9.09E-08	0.00010251	-1.69	-8.41	20p12
9	209822_s_at	VLDLR	-9.20	1.10E-07	0.00011678	-1.61	-8.23	9p24
10	202853_s_at	RYK	4.00	4.44E-09	1.22E-05	1.31	8.09	3q22
11	205055_at	ITGAE	-2.27	3.00E-08	4.79E-05	-1.35	-7.98	17p13
12	239214_at		-5.05	1.32E-07	0.00012654	-1.38	-7.71	
13	242414_at		-4.56	7.33E-08	9.61E-05	-1.32	-7.70	
14	200871_s_at	PSAP	3.28	1.58E-08	2.75E-05	1.18	7.45	10q21-q22
15	221969_at	PAX5	-3.53	2.69E-07	0.00020952	-1.33	-7.40	9p13
16	204328_at	EVER1	2.14	9.37E-09	2.25E-05	1.14	7.37	17q25.3
17	223046_at	EGLN1	4.51	1.24E-08	2.37E-05	1.11	7.19	1q42.1
18	215925_s_at	CD72	-5.99	4.17E-07	0.00023043	-1.26	-7.13	9p13.1
19	221497_x_at	EGLN1	3.67	7.63E-08	9.61E-05	1.12	6.97	1q42.1
20	214022_s_at	MGC27165	4.23	1.60E-07	0.0001392	1.15	6.93	14
21	219033_at	FLJ21308	-3.40	6.01E-07	0.00028321	-1.21	-6.91	5q11.1
22	231887_s_at	KIAA1274	3.30	1.41E-07	0.00012885	1.12	6.86	10q22.1
23	208146_s_at	CPVL	4.46	8.02E-08	9.61E-05	1.08	6.85	7p15-p14
24	228083_at	CACNA2D4	-7.04	5.57E-07	0.00027357	-1.15	-6.77	12p13.33
25	225912_at	TP53INP1	7.38	3.08E-07	0.0002164	1.13	6.73	8q22
26	200989_at	HIF1A	1.96	4.58E-08	6.75E-05	1.03	6.72	14q21-q24
27	204044_at	QPRT	-5.84	2.24E-06	0.00062853	-1.35	-6.71	16p12.1
28	213894_at	KIAA0960	-5.68	1.28E-06	0.00043327	-1.20	-6.68	7p21.3
29	205821_at	D12S2489E	-4.65	1.52E-06	0.00046983	-1.19	-6.61	12p13.2-p12.3
30	203756_at	P164RHOGF	5.83	6.06E-07	0.00028321	1.16	6.61	11q13.2

31	218029_at	FLJ13725	2.50	1.23E-07	0.00012425	1.03	6.61	16q21	
32	220132_s_at	LLT1	-5.09	2.13E-06	0.00061928	-1.20	-6.53	12p13	
33	201601_x_at	MGC27165	5.39	9.10E-07	0.00037507	1.15	6.49		14
34	209170_s_at	GPM6B	-11.50	3.73E-06	0.00079529	-1.32	-6.48	Xp22.2	
35	211991_s_at	HLA-DPA1	3.09	3.60E-07	0.0002164	1.03	6.43	6p21.3	
36	212063_at	CD44	-2.09	4.63E-07	0.00024662	-1.03	-6.41	11p13	
37	200953_s_at	CCND2	5.21	6.23E-07	0.0002846	1.06	6.39	12p13	
38	201065_s_at	GTF2I	-1.96	3.36E-07	0.0002164	-1.00	-6.37	7q11.23	
39	219165_at	PDLIM2	2.37	3.16E-07	0.0002164	1.00	6.33	8p21.2	
40	203435_s_at	MME	30.50	1.86E-06	0.00056668	1.23	6.31	3q25.1-q25.2	
41	225703_at	KIAA1545	-2.01	9.20E-07	0.00037507	-1.03	-6.30	12q24.33	
42	219949_at	LRRRC2	-5.34	3.35E-06	0.00075622	-1.15	-6.29	3p21.31	
43	226496_at	FLJ22611	-2.18	1.95E-07	0.00016262	-0.96	-6.28	9p12	
44	219686_at	HSA250839	9.21	4.82E-07	0.00024979	1.00	6.27	4p16.2	
45	202123_s_at	ABL1	2.13	2.73E-07	0.00020952	0.96	6.24	9q34.1	
46	238022_at		-3.68	1.14E-06	0.00042525	-1.02	-6.24		
47	203569_s_at	OFD1	-1.82	2.04E-06	0.00060862	-1.06	-6.24	Xp22.2-p22.3	
48	201875_s_at	FLJ21047	-1.91	4.21E-07	0.00023043	-0.97	-6.22	1q23.2	
49	211581_x_at	LST1	4.07	1.19E-06	0.00042525	1.04	6.20	6p21.3	
50	55872_at	KIAA1196	3.18	3.41E-07	0.0002164	0.95	6.17	20q13.33	

2.13 kort versus pret

#	affy id	HUGO name	fc	p	q	stn	t	Map-Location
1	232950_s_at	NIR3	2.37	1.85E-06	0.03549483	1.44	6.72	12q24.31
2	203124_s_at	SLC11A2	2.11	2.83E-06	0.03549483	1.38	6.45	12q13
3	225386_s_at	LOC92906	5.48	3.33E-06	0.03549483	1.36	6.36	2p22.2
4	209760_at	KIAA0922	2.44	6.49E-06	0.05195166	1.30	6.08	4q31.3
5	227077_at		2.76	9.90E-06	0.06339581	1.27	5.92	
6	235585_at		2.32	1.24E-05	0.06593254	1.26	5.88	
7	236208_at		3.61	2.33E-05	0.0932046	1.23	5.65	
8	236973_at	MAL	3.17	1.91E-05	0.08724065	1.19	5.57	2cen-q13
9	204005_s_at	PAWR	5.93	5.06E-05	0.13906441	1.24	5.50	12q21
10	205934_at	PLCL1	7.15	8.45E-05	0.13906441	1.31	5.48	2q33
11	228031_at		2.22	2.63E-05	0.09341211	1.17	5.46	
12	218998_at	FLJ20457	2.22	3.53E-05	0.11289431	1.18	5.44	9q31.3
13	203689_s_at	FMR1	2.33	1.00E-04	0.13906441	1.17	5.17	Xq27.3
14	201778_s_at	KIAA0494	2.15	5.89E-05	0.13906441	1.11	5.16	1pter-p22.1
15	201392_s_at	IGF2R	3.13	6.15E-05	0.13906441	1.10	5.12	6q26
16	230672_at		1.63	7.22E-05	0.13906441	1.11	5.12	
17	226106_at	ZFP26	2.45	7.06E-05	0.13906441	1.08	5.04	11p15.3
18	210055_at	TSHR	6.76	0.00012495	0.13906441	1.12	5.02	14q31
19	230414_s_at	LOC124491	-1.97	7.93E-05	0.13906441	-1.07	-5.01	16q22.3
20	202020_s_at	LANCL1	2.34	9.49E-05	0.13906441	1.09	5.01	2q33-q35
21	225591_at	FBXO25	2.12	0.00010652	0.13906441	1.08	4.99	8p23.3

22 227413_at	MGC10067	2.47	7.58E-05	0.13906441	1.07	4.99	5q33.3
23 222701_s_at	MGC2217	3.23	0.00010052	0.13906441	1.08	4.98	8q11.23
24 236104_at		2.52	0.00010129	0.13906441	1.05	4.88	
25 215245_x_at	FMR1	2.43	0.0001267	0.13906441	1.05	4.85	Xq27.3
26 227266_s_at		4.69	0.00010656	0.13906441	1.04	4.85	
27 219474_at	FLJ23186	6.93	0.000173	0.14576411	1.07	4.83	3q13.13
28 218730_s_at	OGN	8.34	0.00024332	0.16845263	1.12	4.82	9q22
29 228009_x_at	ZNRD1	1.84	0.0001103	0.13906441	1.03	4.82	6p21.3
30 210349_at	CAMK4	1.96	0.00013065	0.13906441	1.02	4.77	5q21.3
31 223350_x_at	LIN7C	1.63	0.00013742	0.13906441	1.03	4.77	11p14
32 226223_at		5.11	0.00025415	0.16845263	1.08	4.75	
33 225765_at	KPNB2	2.31	0.00012406	0.13906441	1.01	4.74	5q13.1
34 208848_at	ADH5	3.10	0.00026628	0.16845263	1.09	4.74	4q21-q25
35 225269_s_at	HCC-4	2.35	0.00018007	0.14782865	1.02	4.70	2q24.2
36 219802_at	FLJ22028	2.43	0.00027057	0.16845263	1.07	4.70	12p12.1
37 224946_s_at	MGC12981	1.59	0.00013899	0.13906441	1.00	4.70	2q21.1
38 228830_s_at	ATF7	1.61	0.00013866	0.13906441	1.00	4.70	12q13
39 213878_at	FLJ22028	2.28	0.00014829	0.1396425	1.00	4.68	12p12.1
40 225011_at		-1.99	0.00014465	0.1396425	-1.00	-4.68	
41 211795_s_at	FYB	4.44	0.00020818	0.16257283	1.02	4.67	5p13.1
42 212372_at	MYH10	3.54	0.00034474	0.19030537	1.09	4.66	17p13
43 226269_at		2.08	0.00015637	0.14304412	0.99	4.64	
44 226338_at	DKFZp762O076	1.83	0.00016639	0.1439836	0.99	4.64	8q21.3
45 225385_s_at	LOC92906	3.82	0.00016367	0.1439836	0.99	4.63	2p22.2
46 227525_at	GLCCI1	3.36	0.00018772	0.15025986	0.99	4.60	7p22.1
47 238695_s_at	RAB39B	3.11	0.00025256	0.16845263	0.99	4.57	
48 228615_at	LOC286161	1.81	0.00031547	0.18095547	1.00	4.57	8p23.3
49 222849_s_at	FLJ23142	1.99	0.00026204	0.16845263	0.99	4.54	2q31.1
50 217551_at		4.22	0.00035902	0.19158495	1.02	4.53	

2.14 kort versus prob

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	226496_at	FLJ22611	-14.68	9.80E-12	2.78E-07	-3.11	-14.84	9p12
2	241871_at		13.31	1.11E-08	1.37E-05	2.65	11.89	
3	213539_at	CD3D	28.78	2.56E-08	2.45E-05	2.82	11.63	11q23
4	208690_s_at	PDLIM1	-7.73	2.49E-11	3.53E-07	-2.01	-11.19	10q22-q26.3
5	225314_at	MGC45416	8.16	5.49E-08	4.10E-05	2.49	10.73	4p11
6	202789_at		4.88	2.43E-09	5.74E-06	2.01	10.55	
7	209619_at	CD74	-8.84	5.01E-10	2.37E-06	-1.95	-10.44	5q32
8	232950_s_at	NIR3	4.43	7.32E-10	2.97E-06	1.92	10.44	12q24.31
9	226459_at	FLJ35564	-9.45	2.07E-09	5.60E-06	-2.06	-10.39	10q23.33
10	221969_at	PAX5	-27.24	4.83E-09	8.57E-06	-2.25	-10.35	9p13
11	225563_at	LOC255967	-4.38	2.08E-10	1.40E-06	-1.87	-10.31	13q12.13
12	228046_at	LOC152485	10.98	6.13E-08	4.10E-05	2.26	10.28	4q31.1
13	201015_s_at	JUP	-21.04	1.29E-09	4.57E-06	-1.95	-10.21	17q21

14 221581_s_at	WBSCR5	-14.46	5.35E-09	8.93E-06	-2.11	-10.12	7q11.23
15 226878_at		-4.51	6.66E-11	6.30E-07	-1.78	-10.09	
16 204249_s_at	LMO2	-10.67	5.93E-09	9.34E-06	-1.98	-9.85	11p13
17 217478_s_at	HLA-DMA	-6.90	1.63E-09	5.13E-06	-1.85	-9.84	6p21.3
18 210349_at	CAMK4	4.19	6.73E-08	4.25E-05	1.99	9.62	5q21.3
19 244189_at		2.96	4.39E-08	3.56E-05	1.93	9.58	
20 224710_at	RAB34	-6.71	2.46E-10	1.40E-06	-1.69	-9.56	17q11.1
21 239214_at		-23.04	1.38E-08	1.45E-05	-1.99	-9.54	
22 204069_at	MEIS1	-20.02	1.26E-08	1.43E-05	-1.90	-9.42	2p14-p13
23 238695_s_at	RAB39B	17.50	3.47E-07	0.00012324	2.13	9.20	
24 229029_at		18.33	4.71E-07	0.00014101	2.25	9.13	
25 218942_at	FLJ22055	6.31	6.90E-08	4.26E-05	1.80	9.09	12q13.13
26 226764_at	LOC152485	24.49	4.50E-07	0.00014032	2.13	9.05	4q31.1
27 227077_at		4.04	1.68E-07	7.10E-05	1.82	8.88	
28 215925_s_at	CD72	-56.03	5.86E-08	4.10E-05	-1.95	-8.81	9p13.1
29 212827_at	IGHM	-8.31	2.70E-08	2.45E-05	-1.72	-8.78	14q32.33
30 205689_at	KIAA0435	5.20	3.30E-09	6.69E-06	1.56	8.76	1q42.2
31 209374_s_at	IGHM	-10.98	3.92E-08	3.27E-05	-1.75	-8.72	14q32.33
32 201721_s_at	LAPTM5	-2.39	2.86E-09	6.24E-06	-1.53	-8.65	1p34
33 225703_at	KIAA1545	-2.92	1.01E-08	1.32E-05	-1.57	-8.58	12q24.33
34 225386_s_at	LOC92906	9.27	5.05E-07	0.00014772	1.85	8.55	2p22.2
35 233500_x_at	LLT1	-12.98	7.50E-08	4.53E-05	-1.76	-8.50	12p13
36 219463_at	C20orf103	-40.67	9.44E-08	5.19E-05	-1.81	-8.47	20p12
37 218205_s_at	MKNK2	-3.28	2.69E-08	2.45E-05	-1.60	-8.45	19p13.3
38 202853_s_at	RYK	6.08	5.65E-07	0.00015867	1.81	8.43	3q22
39 204949_at	ICAM3	5.08	4.42E-07	0.00014032	1.76	8.43	19p13.3-p13.2
40 217979_at	NET-6	-7.88	2.76E-08	2.45E-05	-1.58	-8.41	7p21.1
41 212063_at	CD44	-3.66	2.17E-09	5.60E-06	-1.46	-8.38	11p13
42 244261_at	IL28RA	-30.25	1.24E-07	5.78E-05	-1.81	-8.34	1p36.11
43 206674_at	FLT3	-19.39	1.23E-07	5.78E-05	-1.78	-8.33	13q12
44 222895_s_at	BCL11B	18.35	1.10E-06	0.00023312	1.92	8.32	14q32.31
45 203569_s_at	OFD1	-2.62	1.02E-08	1.32E-05	-1.50	-8.30	Xp22.2-p22.3
46 228007_at		5.47	4.44E-07	0.00014032	1.71	8.30	
47 201137_s_at	HLA-DPB1	-5.56	8.81E-09	1.25E-05	-1.46	-8.21	6p21.3
48 203373_at	SOCS2	-5.64	3.71E-09	7.03E-06	-1.41	-8.11	12q
49 226425_at	FLJ21069	4.66	4.72E-08	3.72E-05	1.48	8.09	2p23.2
50 244876_at		-3.64	6.31E-09	9.42E-06	-1.42	-8.08	

2.15 pret versus prob

#	affy id	HUGO name	fc	p	q	stn	t	Map Location
1	226496_at	FLJ22611	-19.63	6.38E-12	2.30E-07	-3.20	-15.07	9p12
2	221969_at	PAX5	-34.79	4.20E-09	2.52E-05	-2.29	-10.43	9p13
3	239214_at		-26.53	1.39E-08	5.03E-05	-2.11	-9.64	
4	226459_at	FLJ35564	-7.02	2.43E-09	2.21E-05	-1.85	-9.45	10q23.33

5	225563_at	LOC255967	-3.75	1.26E-09	2.21E-05	-1.81	-9.38	13q12.13
6	209536_s_at	EHD4	-4.85	2.46E-09	2.21E-05	-1.82	-9.33	15q11.1
7	217478_s_at	HLA-DMA	-6.01	3.20E-09	2.30E-05	-1.74	-8.99	6p21.3
8	215925_s_at	CD72	-88.75	5.30E-08	9.54E-05	-1.98	-8.87	9p13.1
9	233500_x_at	LLT1	-19.45	5.68E-08	9.54E-05	-1.95	-8.81	12p13
10	244876_at		-3.54	1.36E-08	5.03E-05	-1.71	-8.76	
11	204069_at	MEIS1	-12.42	1.40E-08	5.03E-05	-1.73	-8.75	2p14-p13
12	209822_s_at	VLDLR	-12.38	7.74E-08	0.00011249	-1.84	-8.55	9p24
13	226878_at		-3.84	1.61E-08	5.27E-05	-1.66	-8.52	
14	219463_at	C20orf103	-40.41	9.44E-08	0.00013063	-1.84	-8.47	20p12
15	201137_s_at	HLA-DPB1	-7.17	1.04E-08	5.03E-05	-1.61	-8.36	6p21.3
16	203603_s_at	ZFH1B	-8.04	7.82E-08	0.00011249	-1.74	-8.36	2q22
17	225592_at	NRM	-2.79	3.48E-08	8.33E-05	-1.63	-8.25	6p21.31
18	203932_at	HLA-DMB	-4.44	2.01E-08	5.55E-05	-1.60	-8.24	6p21.3
19	208302_at	HB-1	-5.53	6.10E-08	9.54E-05	-1.64	-8.18	5q31.3
20	207697_x_at	LILRB2	-5.85	1.97E-08	5.55E-05	-1.56	-8.11	19q13.4
21	204674_at	LRMP	-5.84	4.72E-08	9.54E-05	-1.60	-8.09	12p12.1
22	211126_s_at	CSRP2	-20.40	1.95E-07	0.00020662	-1.72	-8.02	12q21.1
23	213045_at	KIAA0561	-3.26	2.94E-08	7.55E-05	-1.55	-8.02	19p13.11
24	226789_at		-4.27	3.70E-08	8.33E-05	-1.54	-7.92	
25	235593_at		-8.32	2.57E-07	0.00022613	-1.72	-7.91	
26	35974_at	LRMP	-6.98	5.58E-08	9.54E-05	-1.55	-7.90	12p12.1
27	219033_at	FLJ21308	-5.68	5.90E-08	9.54E-05	-1.53	-7.84	5q11.1
28	206398_s_at	CD19	-18.88	3.17E-07	0.00025947	-1.75	-7.84	16p11.2
29	208306_x_at	HLA-DRB4	-6.60	1.70E-07	0.00018845	-1.54	-7.67	6p21.3
30	218205_s_at	MKNK2	-3.13	5.97E-08	9.54E-05	-1.47	-7.63	19p13.3
31	218469_at	CKTSF1B1	-29.47	5.28E-07	0.00034533	-1.70	-7.57	15q13-q15
32	207030_s_at	CSRP2	-35.86	4.95E-07	0.00033726	-1.65	-7.56	12q21.1
33	205821_at	D12S2489E	-9.13	2.55E-07	0.00022613	-1.53	-7.54	12p13.2-p12.3
34	202481_at	SDR1	-4.49	1.11E-07	0.000143	-1.46	-7.48	1p36.1
35	228754_at	KIAA1719	2.58	2.61E-07	0.00022613	1.45	7.42	3p24-p23
36	202114_at	SNX2	-4.33	2.91E-07	0.00024365	-1.49	-7.42	5q23
37	225703_at	KIAA1545	-2.72	1.04E-07	0.00013838	-1.42	-7.38	12q24.33
38	231902_at	LOC152485	3.19	3.31E-05	0.00497368	1.73	7.37	4q31.1
39	203796_s_at	BCL7A	-3.54	2.64E-07	0.00022613	-1.45	-7.32	12q24.13
40	203569_s_at	OFD1	-2.49	1.45E-07	0.00017383	-1.40	-7.26	Xp22.2-p22.3
41	243756_at		-3.85	1.72E-07	0.00018845	-1.40	-7.25	
42	52164_at	C11orf24	-3.44	1.38E-07	0.00017112	-1.40	-7.25	11q13
43	244261_at	IL28RA	-10.60	2.30E-07	0.00022395	-1.42	-7.24	1p36.11
44	213894_at	KIAA0960	-8.61	4.97E-07	0.00033726	-1.46	-7.22	7p21.3
45	233358_at	FLJ14311	-2.48	2.05E-07	0.00021106	-1.39	-7.18	
46	221866_at	TFEB	-6.08	3.66E-07	0.00028044	-1.42	-7.17	6p21
47	238750_at		-4.93	1.73E-07	0.00018845	-1.38	-7.16	
48	242414_at		-4.10	2.14E-07	0.00021432	-1.38	-7.12	
49	220132_s_at	LLT1	-7.22	8.49E-07	0.00046995	-1.45	-7.06	12p13
50	218217_at	RISC	-5.35	4.54E-07	0.00032678	-1.39	-7.03	17q23.1

Claims

1. A method for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample, the method comprising determining the expression level of markers selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1 and/or 2,

wherein

- 10 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.1

- 15 is indicative for the presence of ball when ball is distinguished from all other subtypes,

and/or wherein

- 20 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.2

is indicative for the presence of cpre when cpre is distinguished from all other subtypes,

and/or wherein

- 25 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 6, 8, 9, 10, 12, 13, 14, 16, 17, 18, 22, 23, 24, 25, 30, 31, 34, 38, 40, 42, 43, 44, 46, 48, and/or 49, of Table 1.3 and/or

a higher expression of at least one polynucleotide defined by any of the numbers 4, 5, 7, 11, 15, 19, 20, 21, 26, 27, 28, 29, 32, 33, 35, 36, 37, 39, 41, 45, 47, and/or 50 of Table 1.3

- 30 is indicative for the presence of cpreh when cpreh is distinguished from all other subtypes,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 20, 21, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, and/or 48, of Table 1.4, and/or

5 a higher expression of at least one polynucleotide defined by any of the numbers 16, 22, 39, 49, and/or 50 of Table 1.4

is indicative for the presence of kort when kort is distinguished from all other subtypes,

and/or wherein

10 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.5

15 is indicative for the presence of pret when pret is distinguished from all other subtypes,

and/or wherein

20 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 6, 8, 9, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 25, 26, 27, 28, 29, 32, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 1.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 5, 7, 10, 20, 22, 23, 24, 30, 31, 33, 34, and/or 39 of Table 1.6,

is indicative for the presence of prob when prob is distinguished from from all other subtypes,

25 and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 4, 8, 10, 12, 15, 17, 20, 23, 24, 25, 27, 28, 29, 30, 31, 34, 36, 37, 40, 42, 44, 45, 46, 49, and/or 50 of Table 2.1, and/or

30 a higher expression of at least one polynucleotide defined by any of the numbers 2, 5, 6, 7, 9, 11, 13, 14, 16, 18, 19, 21, 22, 26, 32, 33, 35, 38, 39, 41, 43, 47, 48,

is indicative for the presence of ball when ball is distinguished from
cpre,

and/or wherein

5 a lower expression of at least one polynucleotide defined by any of the
numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,
21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 38, 39, 40, 41,
42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table of Table 2.2, and/or

a higher expression of at least one polynucleotide defined by any of the
numbers 26, and/or 37, of Table 2.2

10 is indicative for the presence of ball when ball is distinguished from
cpreph,

and/or wherein

15 a lower expression of at least one polynucleotide defined by any of the
numbers 1, 2, 3, 4, 5, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21,
22, 23, 24, 25, 26, 28, 30, 31, 33, 34, 36, 37, 38, 39, 40, 41, 42, 43, 45,
46, 47, 48, and/or 49, of Table 2.3, and/or

a higher expression of at least one polynucleotide defined by any of the
numbers 6, 7, 27, 29, 32, 35, 44, and/or 50 of Table 2.3

20 is indicative for the presence of ball when ball is distinguished from
kort,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the
numbers 3, 5, 6, 7, 13, 17, 18, 19, 21, 22, 26, 27, 30, 32, 34, 36, 38, 40,
47, and/or 48, of Table 2.4, and/or

25 a higher expression of at least one polynucleotide defined by any of the
numbers 1, 2, 4, 8, 9, 10, 11, 12, 14, 15, 16, 20, 23, 24, 25, 28, 29,
31, 33, 35, 37, 39, 41, 42, 43, 44, 45, 46, 49, and/or 50 of Table 2.4

is indicative for the presence of ball when ball is distinguished from
pret,

30 and/or wherein

a lower expression of at least one polynucleotide defined by any of the
numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19,

20, 21, 22, 23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 37, 38, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table of Table 2.5, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 29, 30 and/or 39, of Table 2.5,

5 is indicative for the presence of ball when ball is distinguished from prob,

and/or wherein

10 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 7, 9, 10, 11, 13, 17, 18, 21, 24, 25, 27, 29, 30, 31, 36, 37, 38, 40, 42, 43, 45, 46, 49, and/or 50 of Table 2.6, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 6, 8, 12, 14, 15, 16, 19, 20, 22, 23, 26, 28, 32, 33, 34, 35, 39, 41, 44, 47, and/or 48 of Table 2.6,

15 is indicative for the presence of cpre when cpre is distinguished from cpreph,

and/or wherein

20 a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 6, 8, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 23, 24, 25, 27, 28, 29, 30, 31, 32, 35, 36, 38, 40, 41, 43, 44, 45, 46, 48, 49, and/or 50 of Table 2.7, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 3, 7, 9, 11, 22, 26, 33, 34, 37, 39, 42, 47, of Table 2.7,

is indicative for cpre when cpre is distinguished from kort,

and/or wherein

25 a lower expression of at least one polynucleotide defined by any of the numbers 20, 28, 31, 37, 38, and/or 50 of Table 2.8, and/or

a higher expression of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25, 26, 27, 29, 30, 32, 33, 34, 35, 36, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, and/or 49 of Table 2.8

30 is indicative for cpre when cpre is distinguished from pret,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27, 28, 29, 30, 31, 32, 34, 35, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, and/or 50 of Table 2.9,

5 a higher expression of at least one polynucleotide defined by any of the numbers 26, 33, 41, and/or 49 of Table 2.9

is indicative for cpre when cpre is distinguished from prob,

and/or wherein

10 a lower expression of at least one polynucleotide defined by any of the numbers 3, 6, 12, 17, 23, 28, 34, 35, and/or 41, of Table 2.10, and/or

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 4, 5, 7, 8, 9, 10, 11, 13, 14, 15, 16, 18, 19, 20, 21, 22, 24, 25, 26, 27, 29, 30, 31, 32, 33, 36, 37, 38, 39, 40, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.10

15 is indicative for cpreph when cpreph is distinguished from kort,

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 42, and/or 43, of Table 2.11, and/or

20 a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.11,

is indicative for cpreph when cpreph is distinguished from pret,

and/or wherein

25 a lower expression of at least one polynucleotide defined by any of the numbers 1, 3, 5, 8, 9, 11, 12, 13, 15, 18, 21, 24, 27, 28, 29, 32, 34, 36, 38, 41, 42, 43, 46, 47, 48, of Table 2.12, and/or

30 a higher expression of at least one polynucleotide defined by any of the numbers 2, 4, 6, 7, 10, 14, 16, 17, 19, 20, 22, 23, 25, 26, 30, 31, 33, 35, 37, 39, 40, 44, 45, 49, and/or 50 of Table 2.12

is indicative for cpreph when cpreph is distinguished from prob

and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 19, and/or 40, of Table 2.13

a higher expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.13,

is indicative for kort when kort is distinguished from pret,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 4, 7, 9, 10, 11, 13, 14, 15, 16, 17, 20, 21, 22, 28, 29, 31, 32, 33, 35, 36, 37, 40, 41, 42, 43, 45, 47, 48, and/or 50 of Table 2.14,
and/or

a higher expression of at least one polynucleotide defined by any of the numbers 2, 3, 5, 6, 8, 12, 18, 19, 23, 24, 25, 26, 27, 30, 34, 38, 39, 44, 46, and/or 49, of Table 2.14

is indicative for kort when kort is distinguished from prob,
and/or wherein

a lower expression of at least one polynucleotide defined by any of the numbers 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, and/or 50 of Table 2.15,

is indicative for pret when pret is distinguished from prob.

2. The method according to claim 1 wherein the polynucleotide is labelled.

3. The method according to claim 1 or 2, wherein the label is a luminescent, preferably a fluorescent label, an enzymatic or a radioactive label.

4. The method according at least one of the claims 1-3, wherein the expression level of at least two, preferably of at least ten, more preferably of at least

25, most preferably of 50 of the markers of at least one of the Tables 1 and/or 2 is determined.

- 5 5. The method according to at least one of the claims 1-4, wherein the expression level of markers expressed lower in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold lower, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold lower in the first subtype.
- 10
6. The method according to at least one of the claims 1-4, wherein the expression level of markers expressed higher in a first subtype than in at least one second subtype, which differs from the first subtype, is at least 5 %, 10% or 20%, more preferred at least 50% or may even be 75% or 100%, i.e. 2-fold higher, preferably at least 10-fold, more preferably at least 50-fold, and most preferably at least 100-fold higher in the first subtype.
- 15
7. The method according to at least one of the claims 1-6, wherein the sample is from an individual having ALL.
- 20
8. The method according to at least one of the claims 1-7, wherein at least one polynucleotide is in the form of a transcribed polynucleotide, or a portion thereof.
- 25 9. The method according to claim 8, wherein the transcribed polynucleotide is a mRNA or a cDNA.
10. The method according to claim 8 or 9, wherein the determining of the expression level comprises hybridizing the transcribed polynucleotide to a

complementary polynucleotide, or a portion thereof, under stringent hybridization conditions.

- 5 11. The method according to at least one of the claims 1-7, wherein at least one polynucleotide is in the form of a polypeptide, or a portion thereof.
- 10 12. The method according to at least one of the claims 8, 9 or 12, wherein the determining of the expression level comprises contacting the polynucleotide or the polypeptide with a compound specifically binding to the polynucleotide or the polypeptide.
13. The method according to claim 12, wherein the compound is an antibody, or a fragment thereof.
- 15 14. The method according to at least one of the claims 1-13, wherein the method is carried out on an array.
- 20 15. The method according to at least one of the claims 1-14, wherein the method is carried out in a robotics system.
- 25 16. The method according to at least one of the claims 1-15, wherein the method is carried out using microfluidics.
17. Use of at least one marker as defined in at least one of the claims 1-3 for the manufacturing of a diagnostic for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL.

18. The use according to claim 17 for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in an individual having ALL.
- 5
19. A diagnostic kit containing at least one marker as defined in at least one of the claims 1-3 for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL, in combination with suitable auxiliaries.
- 10
20. The diagnostic kit according to claim 19, wherein the kit contains a reference for the immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL.
- 15
21. The diagnostic kit according to claim 20, wherein the reference is a sample or a data bank.
- 20
22. An apparatus for distinguishing immunologically defined ALL subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature T-ALL, and/or T-ALL in a sample containing a reference data bank.
- 25
23. The apparatus according to claim 22, wherein the reference data bank is obtainable by comprising
- 30
- (a) compiling a gene expression profile of a patient sample by determining the expression level of at least one marker selected from the markers identifiable by their Affymetrix Identification Numbers (affy id) as defined in Tables 1, and/or 2, and

(b) classifying the gene expression profile by means of a machine learning algorithm.

24. The apparatus according to claim 23, wherein the machine learning
5 algorithm is selected from the group consisting of Weighted Voting, K-
Nearest Neighbors, Decision Tree Induction, Support Vector Machines, and
Feed-Forward Neural Networks, preferably Support Vector Machines.
25. The apparatus according to at least one of the claims 22-24, wherein the
10 apparatus contains a control panel and/or a monitor.
26. A reference data bank for distinguishing immunologically defined ALL
subtypes Pro-B-ALL, c-ALL, Pre-B-ALL, c-ALL/Pre-B-ALL, mature B-
ALL, precursor B-ALL, Pro-T-ALL, Pre-T-ALL, cortical T-ALL, mature
15 T-ALL, and/or T-ALL obtainable by comprising
(a) compiling a gene expression profile of a patient sample by
determining the expression level of at least one marker selected
from the markers identifiable by their Affymetrix Identification
Numbers (affy id) as defined in Tables 1, and/or 2, and
20 (b) classifying the gene expression profile by means of a machine
learning algorithm.
27. The reference data bank according to claim 26, wherein the reference data
bank is backed up and/or contained in a computational memory chip.